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A1

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(74) Agent: VANCE, David, H.; The Du Pont Merck Pharmaceutical Company, Legal/Patent Records Center, 1007 Market Street, Wilmington, DE 19898 (US).

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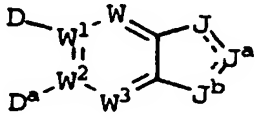
(54) Title: AMIDINOINDOLES, AMIDINOAZOLES, AND ANALOGS THEREOF AS INHIBITORS OF FACTOR Xa AND OF THROMBIN

(57) Abstract

The present application describes amidinoindoles, amidinoazoles, and analogs thereof of formula (I): wherein W, W^1, W^2, and W^3 are selected from CH and N, provided that one of W^1 and W^2 is C(C(=NH)NH_2) and at most two of W, W^1, W^2, and W^3 are N and one of J^a and J^b is substituted by -$(CH_2)_n$-Z-A-B, which are useful as inhibitors of factor Xa or thrombin.



(I)

Express Mail No. EF378134428US

*(Referred to in PCT Gazette No. 42/1998, Section II)

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INTERNATIONAL SEARCH REPORT

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

The vast number of theoretically conceivable compounds comprised under formula(I) of claim 1 precludes a comprehensive documentary search as well as a comprehensive on line search in a structure data base and would not be economically justified (cf. Arts. 6,15 and Rule 33 PCT; see Guidelines B III 2.1).
Based upon the preferred type of substituent for D and Da, the latter search was limited to compounds of formula (I) wherein either D or Da is an amidino group.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internatio. ·l Application No
PCT/US 97/11325

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 540051 A	05-05-93	AT 136293 T	15-04-96
		AU 666137 B	01-02-96
		AU 2747092 A	06-05-93
		CA 2081836 A	01-05-93
		CN 1072677 A	02-06-93
		DE 69209615 D	09-05-96
		DE 69209615 T	09-01-97
		ES 2088073 T	01-08-96
		FI 924932 A	01-05-93
		HR 921147 A	31-10-95
		HU 65890 A	28-07-94
		JP 5208946 A	20-08-93
		MX 9206295 A	01-08-93
		NZ 244936 A	26-05-95
		PL 170312 B	29-11-96
		US 5576343 A	19-11-96
		US 5620991 A	15-04-97
		ZA 9208276 A	06-05-93

INTERNATIONAL SEARCH REPORT

Internatio Application No
PCT/US 97/11325

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D235/06 A61K31/395 C07D403/10 C07D471/04 C07D401/06
C07D209/08 C07D209/16 C07D401/12 C07D209/14 C07D231/12
C07D231/56

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
A	EP 0 540 051 A (DAIICHI PHARMACEUTICAL CO.,LTD.) 5 May 1993 cited in the application see claims	1,16
A	R.R. TIDWELL ET AL.: "Aromatic amidines: ..." JOURNAL OF MEDICINAL CHEMISTRY., vol. 262, - 1983 WASHINGTON US, pages 294-298, XP002044077 cited in the application see page 295-296	1,16

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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1

Date of the actual completion of the international search
20 October 1997

Date of mailing of the international search report
04. 11. 97

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NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer
Van Bijlen, H

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INTERNATIONAL SEARCH REPORT

Interr. ...nal application No.
PCT/US 97/ 11325

Box I Observations where certain claims were f und unsearchabl (Continuation of item 1 of fir t sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons

1 [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely

Remark: Although claim(s) 19-20
is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: 1
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically

see annex

3. [ ] Claims Nos..
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6 4(a)

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Int[illegible]nal application No.
PCT/US 97/ 11325

Box I Observations wh re certain claims w r found unsearchable (Continuati n of item 1 f first sheet)

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because they relate to subject matter not required to be searched by this Authority, namely:

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because they relate to parts of the international Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see annex

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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Date of the actual completion of the international search	Date of mailing of the international search report
1 September 1998	03. 09. 98

Name and mailing address of the ISA	Authorized officer
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Information on patent family members

Interm. .. . Application No
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

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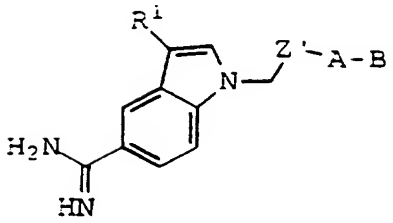
Based upon the preferred type of substituent for D and Da, the latter search was limited to compounds of formula (I) wherein either D or Da is an amidino group.

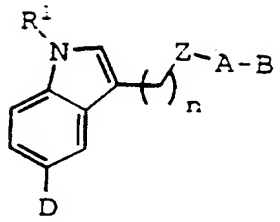
Table 7



Ex	R^1	Z'	A	B	MS or HRMS
101	H	C(O)	1-piperidine	4-benzyl	375.218
102	H	$CH_2C(O)$	1-piperidine	4-benzyl	389.231
103	H	C(O)	1-piperidine	4-(3-F)benzyl	393.209
104	H	$C(O)N(CH_2CO_2CH_3)$	benzyl	4-amidino	218
105	CH_2-CO_2Me	C(O)	1-piperidine	4-benzyl	447.242
106	CH_2-CH_2OH	C(O)	1-piperidine	4-benzyl	419.245
107	CH_2-CO_2H	C(O)	1-piperidine	4-benzyl	433
108	H	C(O)NH	4-piperidine	1-benzyl	390.229
109	H	C(O)	1-piperidine	4-benzoyl	389.198
110	H	C(O)	1-piperazinyl	4-(3-F)benzyl	394.205
111	H	C(O)NH	benzyl	4-phenyl	383.190
112	CH=CH-CO_2Me	C(O)	piperidine	4-benzyl	459
113	H	C(O)	piperidine	4-(2-F)benzyl	393.209

5

Tabl 8a*



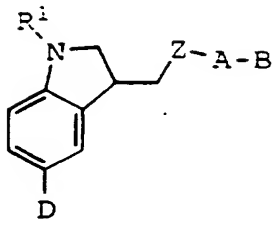
Ex	D	R^1	Z	A	B	MS or HRMS
201	Am	H	C(O)-CH_2NH	phenyl	4-cyclohexyl	389.232
202	Am	H	C(O)	1-piperazinyl	4-p-toluenesulfonyl	440.176
203	Am	H	C(O)NH	2-pyridyl	4-(2-aminosulfonyl) phenyl	449.139
204	Am	H	C(O)NH	1-phenyl	4-(2-tetrazol-5-yl)phenyl	437.187
205	Am	H	C(O)NH	1-phenyl	4-phenyl	369.171
206	Am	H	C(O)	1-piperazinyl	4-phenyl-methylsulfonyl	440.176
207	Am	H	C(O)NH	1-phenyl	4-cyclohexyl	375.218
208	Am	H	C(O)	1-piperazinyl	4-benzyl	376.214
209	Am	Me	C(O)N-($CH_2CO_2CH_3$)	benzyl	3-amidino	435.217
210	Am	Me	C(O)N-($CH_2CO_2CH_3$)	benzyl	4-amidino	435,213
211	Am	Me	C(O)NH	benzyl	4-(2-aminosulfonyl) phenyl	476
212	Am	Me	C(O)NH	benzyl	4-phenyl	397.205
213	Am	Me	$C(O)CH_2$	1-piperazinyl	4-benzyl	389.235

214	Am	H	C(O)NH	phenyl	4-(2-aminosulfonyl) phenyl	448.144
215	Am	H	C(O)	4-piperidinyl	1-benzyl	390.230
216	Am	H	C(O)	1-piperazinyl	4-phenyl	362.197
217	Am	H	C(O)	1-piperidinyl	4-benzyl	374.210
218	Am	Me	C(O)NH	2-pyridyl	5-(2-aminosulfonyl) phenyl	463.155
219	CN	H	C(O)NH	2-Br-phenyl	4-(2-aminosulfonyl) phenyl	526.054
220	CH_3-NH	H	C(O)NH	2-Me-phenyl	4-(2-aminosulfonyl) phenyl	449.164
221	Am	H	C(O)NH	2-F-phenyl	4-(2-aminosulfonyl) phenyl	466.134
222	CN	H	C(O)NH	2-Cl-phenyl	4-(2-aminosulfonyl) phenyl	482.104
223	CN	H	C(O)NH	2-I-phenyl	4-(2-aminosulfonyl) phenyl	574.043
224	Am	H	C(O)NH	2-Me-phenyl	4-(2-aminosulfonyl) phenyl	462.156
225	Am	H	C(O)NH	2-Me-phenyl	4-(2-t-Bu-aminosulfonyl) phenyl	518.222
226	Am	H	(CH_3O-C(O)-CH_2)CH	phenyl	4-(2-aminosulfonyl) phenyl	520.165

227	Am	H	(phenyl $-CH_2$)CH	phenyl	4-(2-aminosulfonyl) phenyl	538.191
228	Am	H	C(O)NH	2-pyridyl	4-(2-CF_3-phenyl)	438.152
229	Am	H	C(O)NH	phenyl	4-(2-ethylaminosulfonyl)phenyl	476.176
230	Am	H	C(O)NH	phenyl	4-(2-propylamino-sulfonyl)phenyl	490.191
231	Am	H	C(O)NH (R^1=2-methyl)	2-I-phenyl	4-(2-aminosulfonyl) phenyl	558.057
232	Am	H	C(O)NH (R^1=2-methyl)	phenyl	4-(2-aminosulfonyl) phenyl	462
233	Am	H	C(O)-NCH_3	phenyl	4-(2-aminosulfonyl) phenyl	462
234	CH_3O	H	C(O)NH (R^1=2-methyl)	phenyl	4-(2-t-Bu-aminosulfonyl) phenyl	506
235	Am	H	C(O)-NCH_3	phenyl	4-(2-methylamino-sulfonyl)phenyl	462.160

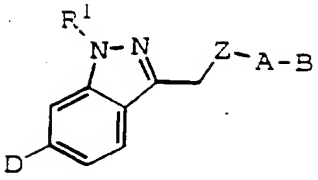
*For all Examples, but 226 and 277, n=1. For Examples 226 and 227, n=0.

Table 8b



Ex	D	R^1	Z	A	B	MS or HRMS
236	CN	H	C(O)NH	phenyl	4-(2-n-Bu-aminosulfonyl) phenyl	
237	Am	H	C(O)NH	phenyl	4-(2-propylamino-sulfonyl)phenyl	492.208
238 (-)	Am	H	C(O)NH	2-pyridyl	4-(2-aminosulfonyl) phenyl	451.154
239	Am	H	C(O)NH	2-pyridyl	4-(2-aminosulfonyl) phenyl	451.155
240	Am	H	C(O)NH	phenyl	4-(2-N,N-dimethylamino-sulfonyl)phenyl	450.160
241 (+)	Am	H	C(O)NH	2-pyridyl	4-(2-t-Bu-amino-sulfonyl)phenyl	507.218
242 (-)	Am	H	C(O)NH	2-pyridyl	4-(2-t-Bu-amino-sulfonyl)phenyl	507.218
243	NH_2-C(O)	H	C(O)NH	2-pyridyl	4-(2-aminosulfonyl) phenyl	451.154
244	Am	H	C(O)NH	phenyl	4-(2-t-Bu-amino-sulfonyl)phenyl	506.4
245	Am	H	C(O)NH	2-pyridyl	4-(2-t-Bu-amino-sulfonyl)phenyl	507.4

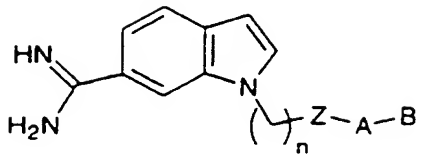
Table 8c



Ex	D	R^1	Z	A	B	MS or HRMS
246	Am	H	C(O)NH	2-pyridyl	4-(2-aminosulfonyl) phenyl	450.135
247	Am	H	C(O)NH	phenyl	4-(2-aminosulfonyl) phenyl	449.139
248	Am	H	C(O)NH	2-pyridyl	4-(2-t-Bu-amino-sulfonyl)phenyl	450.135
249	Am	H	C(O)NH	phenyl	4-(2-t-Bu-amino-sulfonyl)phenyl	505.203

5

Table 9

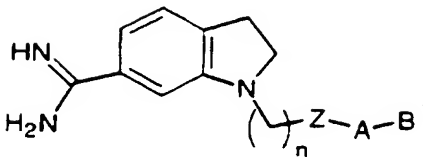


Ex	n	Z	A-B
301	1	C(O)	4-(2-aminosulfonylphenyl)phenyl
302	1	C(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
303	1	C(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
304	1	C(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
305	1	C(O)	2-aminosulfonyl-4-cyclohexylphenyl
306	1	C(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
307	1	C(O)	2-(5-indazol-5-yl)furanyl
308	1	C(O)	2-(5-indazol-6-yl)thienyl
309	1	C(O)	4-(2-tetrazolylphenyl)phenyl
310	1	C(O)NH	4-(2-aminosulfonylphenyl)phenyl
311	1	C(O)NH	4-(2-aminosulfonylphenyl)-2-pyridyl
312	1	C(O)NH	4-(2-methylaminosulfonyl-phenyl)phenyl
313	1	C(O)NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
314	1	C(O)NH	2-aminosulfonyl-4-cyclohexylphenyl
315	1	C(O)NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
316	1	C(O)NH	2-(5-indazol-5-yl)furanyl
317	1	C(O)NH	2-(5-indazol-6-yl)thienyl

318	1	C(O)NH	4-(2-tetrazolylphenyl)phenyl
319	1	NHC(O)	4-(2-aminosulfonylphenyl)phenyl
320	1	NHC(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
321	1	NHC(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
322	1	NHC(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
323	1	NHC(O)	2-aminosulfonyl-4-cyclohexylphenyl
324	1	NHC(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
325	1	NHC(O)	2-(5-indazol-5-yl)furanyl
326	1	NHC(O)	2-(5-indazol-6-yl)thienyl
327	1	NHC(O)	4-(2-tetrazolylphenyl)phenyl
328	1	SO_2NH	4-(2-aminosulfonylphenyl)phenyl
329	1	SO_2NH	4-(2-aminosulfonylphenyl)-2-pyridyl
330	1	SO_2NH	4-(2-methylaminosulfonyl-phenyl)phenyl
331	1	SO_2NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
332	1	SO_2NH	2-aminosulfonyl-4-cyclohexylphenyl
333	1	SO_2NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
334	1	SO_2NH	2-(5-indazol-5-yl)furanyl
335	1	SO_2NH	2-(5-indazol-6-yl)thienyl
336	1	SO_2NH	4-(2-tetrazolylphenyl)phenyl
337	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
338	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl

339	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
340	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
341	0	$CH(CH_2CH_2OH)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
342	0	$CH(CH_2CH_2OH)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
343	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-5-yl)furanyl
344	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-6-yl)thienyl
345	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-tetrazolylphenyl)phenyl
346	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
347	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
348	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
349	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
350	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
351	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
352	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-5-yl)furanyl
353	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-6-yl)thienyl
354	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-tetrazolylphenyl)phenyl

Table 10

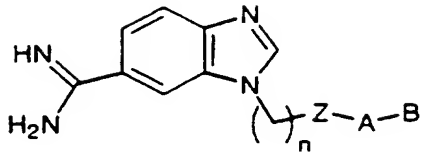


Ex	n	Z	A-B
401	1	C(O)	4-(2-aminosulfonylphenyl)phenyl
402	1	C(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
403	1	C(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
404	1	C(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
405	1	C(O)	2-aminosulfonyl-4-cyclohexylphenyl
406	1	C(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
407	1	C(O)	2-(5-indazol-5-yl)furanyl
408	1	C(O)	2-(5-indazol-6-yl)thienyl
409	1	C(O)	4-(2-tetrazolylphenyl)phenyl
410	1	C(O)NH	4-(2-aminosulfonylphenyl)phenyl
411	1	C(O)NH	4-(2-aminosulfonylphenyl)-2-pyridyl
412	1	C(O)NH	4-(2-methylaminosulfonyl-phenyl)phenyl
413	1	C(O)NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
414	1	C(O)NH	2-aminosulfonyl-4-cyclohexylphenyl
415	1	C(O)NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
416	1	C(O)NH	2-(5-indazol-5-yl)furanyl
417	1	C(O)NH	2-(5-indazol-6-yl)thienyl

418	1	C(O)NH	4-(2-tetrazolylphenyl)phenyl
419	1	NHC(O)	4-(2-aminosulfonylphenyl)phenyl
420	1	NHC(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
421	1	NHC(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
422	1	NHC(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
423	1	NHC(O)	2-aminosulfonyl-4-cyclohexylphenyl
424	1	NHC(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
425	1	NHC(O)	2-(5-indazol-5-yl)furanyl
426	1	NHC(O)	2-(5-indazol-6-yl)thienyl
427	1	NHC(O)	4-(2-tetrazolylphenyl)phenyl
428	1	SO_2NH	4-(2-aminosulfonylphenyl)phenyl
429	1	SO_2NH	4-(2-aminosulfonylphenyl)-2-pyridyl
430	1	SO_2NH	4-(2-methylaminosulfonyl-phenyl)phenyl
431	1	SO_2NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
432	1	SO_2NH	2-aminosulfonyl-4-cyclohexylphenyl
433	1	SO_2NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
434	1	SO_2NH	2-(5-indazol-5-yl)furanyl
435	1	SO_2NH	2-(5-indazol-6-yl)thienyl
436	1	SO_2NH	4-(2-tetrazolylphenyl)phenyl
437	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
438	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl

439	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
440	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
441	0	$CH(CH_2CH_2OH)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
442	0	$CH(CH_2CH_2OH)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
443	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-5-yl)furanyl
444	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-6-yl)thienyl
445	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-tetrazolylphenyl)phenyl
446	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
447	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
448	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
449	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
450	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
451	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
452	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-5-yl)furanyl
453	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-6-yl)thienyl
454	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-tetrazolylphenyl)phenyl

Table 11

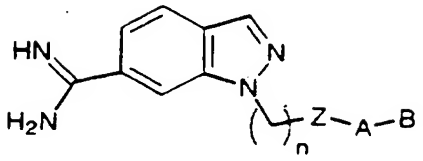


Ex	n	Z	A-B
501	1	C(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
502	1	C(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
503	1	C(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
504	1	C(O)	2-aminosulfonyl-4-cyclohexylphenyl
505	1	C(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
506	1	C(O)	2-(5-indazol-5-yl)furanyl
507	1	C(O)	2-(5-indazol-6-yl)thienyl
508	1	C(O)	4-(2-tetrazolylphenyl)phenyl
509	1	C(O)NH	4-(2-aminosulfonylphenyl)-2-pyridyl
510	1	C(O)NH	4-(2-methylaminosulfonyl-phenyl)phenyl
511	1	C(O)NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
512	1	C(O)NH	2-aminosulfonyl-4-cyclohexylphenyl
513	1	C(O)NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
514	1	C(O)NH	2-(5-indazol-5-yl)furanyl
515	1	C(O)NH	2-(5-indazol-6-yl)thienyl
516	1	C(O)NH	4-(2-tetrazolylphenyl)phenyl
517	1	NHC(O)	4-(2-aminosulfonylphenyl)phenyl

518	1	NHC(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
519	1	NHC(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
520	1	NHC(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
521	1	NHC(O)	2-aminosulfonyl-4-cyclohexylphenyl
522	1	NHC(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
523	1	NHC(O)	2-(5-indazol-5-yl)furanyl
524	1	NHC(O)	2-(5-indazol-6-yl)thienyl
525	1	NHC(O)	4-(2-tetrazolylphenyl)phenyl
526	1	SO_2NH	4-(2-aminosulfonylphenyl)phenyl
527	1	SO_2NH	4-(2-aminosulfonylphenyl)-2-pyridyl
528	1	SO_2NH	4-(2-methylaminosulfonyl-phenyl)phenyl
529	1	SO_2NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
530	1	SO_2NH	2-aminosulfonyl-4-cyclohexylphenyl
531	1	SO_2NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
532	1	SO_2NH	2-(5-indazol-5-yl)furanyl
533	1	SO_2NH	2-(5-indazol-6-yl)thienyl
534	1	SO_2NH	4-(2-tetrazolylphenyl)phenyl
535	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
536	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
537	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
538	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl

539	0	$CH(CH_2CH_2OH)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
540	0	$CH(CH_2CH_2OH)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
541	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-5-yl)furanyl
542	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-6-yl)thienyl
543	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-tetrazolylphenyl)phenyl
544	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
545	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
546	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
547	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
548	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
549	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
550	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-5-yl)furanyl
551	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-6-yl)thienyl
552	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-tetrazolylphenyl)phenyl

Table 12

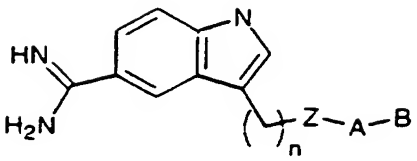


Ex	n	Z	A-B
601	1	C(O)	4-(2-aminosulfonylphenyl)phenyl
602	1	C(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
603	1	C(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
604	1	C(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
605	1	C(O)	2-aminosulfonyl-4-cyclohexylphenyl
606	1	C(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
607	1	C(O)	2-(5-indazol-5-yl)furanyl
608	1	C(O)	2-(5-indazol-6-yl)thienyl
609	1	C(O)	4-(2-tetrazolylphenyl)phenyl
610	1	C(O)NH	4-(2-aminosulfonylphenyl)phenyl
611	1	C(O)NH	4-(2-aminosulfonylphenyl)-2-pyridyl
612	1	C(O)NH	4-(2-methylaminosulfonyl-phenyl)phenyl
613	1	C(O)NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
614	1	C(O)NH	2-aminosulfonyl-4-cyclohexylphenyl
615	1	C(O)NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
616	1	C(O)NH	2-(5-indazol-5-yl)furanyl
617	1	C(O)NH	2-(5-indazol-6-yl)thienyl

618	1	C(O)NH	4-(2-tetrazolylphenyl)phenyl
619	1	NHC(O)	4-(2-aminosulfonylphenyl)phenyl
620	1	NHC(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
621	1	NHC(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
622	1	NHC(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
623	1	NHC(O)	2-aminosulfonyl-4-cyclohexylphenyl
624	1	NHC(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
625	1	NHC(O)	2-(5-indazol-5-yl)furanyl
626	1	NHC(O)	2-(5-indazol-6-yl)thienyl
627	1	NHC(O)	4-(2-tetrazolylphenyl)phenyl
628	1	SO_2NH	4-(2-aminosulfonylphenyl)phenyl
629	1	SO_2NH	4-(2-aminosulfonylphenyl)-2-pyridyl
630	1	SO_2NH	4-(2-methylaminosulfonyl-phenyl)phenyl
631	1	SO_2NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
632	1	SO_2NH	2-aminosulfonyl-4-cyclohexylphenyl
633	1	SO_2NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
634	1	SO_2NH	2-(5-indazol-5-yl)furanyl
635	1	SO_2NH	2-(5-indazol-6-yl)thienyl
636	1	SO_2NH	4-(2-tetrazolylphenyl)phenyl
637	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
638	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl

639	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
640	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
641	0	$CH(CH_2CH_2OH)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
642	0	$CH(CH_2CH_2OH)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
643	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-5-yl)furanyl
644	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-6-yl)thienyl
645	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-tetrazolylphenyl)phenyl
646	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
647	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
648	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
649	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
650	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
651	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
652	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-5-yl)furanyl
653	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-6-yl)thienyl
654	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-tetrazolylphenyl)phenyl

Table 13

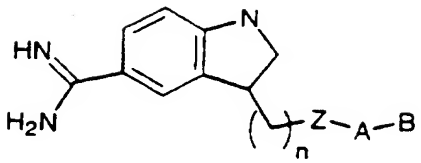


Ex	n	Z	A-B
701	1	C(O)	4-(2-aminosulfonylphenyl)phenyl
702	1	C(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
703	1	C(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
704	1	C(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
705	1	C(O)	2-aminosulfonyl-4-cyclohexylphenyl
706	1	C(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
707	1	C(O)	2-(5-indazol-5-yl)furanyl
708	1	C(O)	2-(5-indazol-6-yl)thienyl
709	1	C(O)	4-(2-tetrazolylphenyl)phenyl
710	1	C(O)NH	4-(2-methylaminosulfonyl-phenyl)phenyl
711	1	C(O)NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
712	1	C(O)NH	2-aminosulfonyl-4-cyclohexylphenyl
713	1	C(O)NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
714	1	C(O)NH	2-(5-indazol-5-yl)furanyl
715	1	C(O)NH	2-(5-indazol-6-yl)thienyl
716	1	C(O)NH	4-(2-tetrazolylphenyl)phenyl
717	1	NHC(O)	4-(2-aminosulfonylphenyl)phenyl

718	1	NHC(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
719	1	NHC(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
720	1	NHC(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
721	1	NHC(O)	2-aminosulfonyl-4-cyclohexylphenyl
722	1	NHC(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
723	1	NHC(O)	2-(5-indazol-5-yl)furanyl
724	1	NHC(O)	2-(5-indazol-6-yl)thienyl
725	1	NHC(O)	4-(2-tetrazolylphenyl)phenyl
726	1	SO_2NH	4-(2-aminosulfonylphenyl)phenyl
727	1	SO_2NH	4-(2-aminosulfonylphenyl)-2-pyridyl
728	1	SO_2NH	4-(2-methylaminosulfonyl-phenyl)phenyl
729	1	SO_2NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
730	1	SO_2NH	2-aminosulfonyl-4-cyclohexylphenyl
731	1	SO_2NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
732	1	SO_2NH	2-(5-indazol-5-yl)furanyl
733	1	SO_2NH	2-(5-indazol-6-yl)thienyl
734	1	SO_2NH	4-(2-tetrazolylphenyl)phenyl
735	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
736	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
737	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
738	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl

739	0	$CH(CH_2CH_2OH)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
740	0	$CH(CH_2CH_2OH)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
741	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-5-yl)furanyl
742	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-6-yl)thienyl
743	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-tetrazolylphenyl)phenyl
744	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
745	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
746	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
747	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
748	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
749	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
750	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-5-yl)furanyl
751	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-6-yl)thienyl
752	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-tetrazolylphenyl)phenyl

Table 14

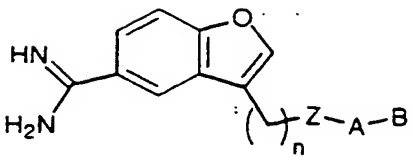


Ex	n	Z	A-B
801	1	C(O)	4-(2-aminosulfonylphenyl)phenyl
802	1	C(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
803	1	C(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
804	1	C(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
805	1	C(O)	2-aminosulfonyl-4-cyclohexylphenyl
806	1	C(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
807	1	C(O)	2-(5-indazol-5-yl)furanyl
808	1	C(O)	2-(5-indazol-6-yl)thienyl
809	1	C(O)	4-(2-tetrazolylphenyl)phenyl
810	1	C(O)NH	4-(2-aminosulfonylphenyl)phenyl
811	1	C(O)NH	4-(2-aminosulfonylphenyl)-2-pyridyl
812	1	C(O)NH	4-(2-methylaminosulfonyl-phenyl)phenyl
813	1	C(O)NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
814	1	C(O)NH	2-aminosulfonyl-4-cyclohexylphenyl
815	1	C(O)NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
816	1	C(O)NH	2-(5-indazol-5-yl)furanyl
817	1	C(O)NH	2-(5-indazol-6-yl)thienyl

818	1	C(O)NH	4-(2-tetrazolylphenyl)phenyl
819	1	NHC(O)	4-(2-aminosulfonylphenyl)phenyl
820	1	NHC(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
821	1	NHC(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
822	1	NHC(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
823	1	NHC(O)	2-aminosulfonyl-4-cyclohexylphenyl
824	1	NHC(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
825	1	NHC(O)	2-(5-indazol-5-yl)furanyl
826	1	NHC(O)	2-(5-indazol-6-yl)thienyl
827	1	NHC(O)	4-(2-tetrazolylphenyl)phenyl
828	1	SO_2NH	4-(2-aminosulfonylphenyl)phenyl
829	1	SO_2NH	4-(2-aminosulfonylphenyl)-2-pyridyl
830	1	SO_2NH	4-(2-methylaminosulfonyl-phenyl)phenyl
831	1	SO_2NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
832	1	SO_2NH	2-aminosulfonyl-4-cyclohexylphenyl
833	1	SO_2NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
834	1	SO_2NH	2-(5-indazol-5-yl)furanyl
835	1	SO_2NH	2-(5-indazol-6-yl)thienyl
836	1	SO_2NH	4-(2-tetrazolylphenyl)phenyl
837	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
838	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl

839	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
840	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
841	0	$CH(CH_2CH_2OH)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
842	0	$CH(CH_2CH_2OH)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
843	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-5-yl)furanyl
844	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-6-yl)thienyl
845	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-tetrazolylphenyl)phenyl
846	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
847	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
848	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
849	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
850	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
851	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
852	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-5-yl)furanyl
853	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-6-yl)thienyl
854	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-tetrazolylphenyl)phenyl

Table 15

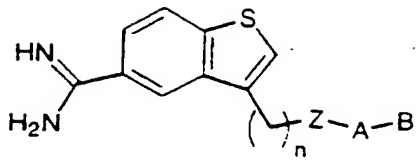


Ex	n	Z	A-B
901	1	C(O)	4-(2-aminosulfonylphenyl)phenyl
902	1	C(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
903	1	C(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
904	1	C(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
905	1	C(O)	2-aminosulfonyl-4-cyclohexylphenyl
906	1	C(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
907	1	C(O)	2-(5-indazol-5-yl)furanyl
908	1	C(O)	2-(5-indazol-6-yl)thienyl
909	1	C(O)	4-(2-tetrazolylphenyl)phenyl
910	1	C(O)NH	4-(2-aminosulfonylphenyl)phenyl
911	1	C(O)NH	4-(2-aminosulfonylphenyl)-2-pyridyl
912	1	C(O)NH	4-(2-methylaminosulfonyl-phenyl)phenyl
913	1	C(O)NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
914	1	C(O)NH	2-aminosulfonyl-4-cyclohexylphenyl
915	1	C(O)NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
916	1	C(O)NH	2-(5-indazol-5-yl)furanyl
917	1	C(O)NH	2-(5-indazol-6-yl)thienyl

918	1	C(O)NH	4-(2-tetrazolylphenyl)phenyl
919	1	NHC(O)	4-(2-aminosulfonylphenyl)phenyl
920	1	NHC(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
921	1	NHC(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
922	1	NHC(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
923	1	NHC(O)	2-aminosulfonyl-4-cyclohexylphenyl
924	1	NHC(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
925	1	NHC(O)	2-(5-indazol-5-yl)furanyl
926	1	NHC(O)	2-(5-indazol-6-yl)thienyl
927	1	NHC(O)	4-(2-tetrazolylphenyl)phenyl
928	1	SO_2NH	4-(2-aminosulfonylphenyl)phenyl
929	1	SO_2NH	4-(2-aminosulfonylphenyl)-2-pyridyl
930	1	SO_2NH	4-(2-methylaminosulfonyl-phenyl)phenyl
931	1	SO_2NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
932	1	SO_2NH	2-aminosulfonyl-4-cyclohexylphenyl
933	1	SO_2NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
934	1	SO_2NH	2-(5-indazol-5-yl)furanyl
935	1	SO_2NH	2-(5-indazol-6-yl)thienyl
936	1	SO_2NH	4-(2-tetrazolylphenyl)phenyl
937	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
938	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl

939	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
940	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
941	0	$CH(CH_2CH_2OH)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
942	0	$CH(CH_2CH_2OH)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
943	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-5-yl)furanyl
944	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-6-yl)thienyl
945	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-tetrazolylphenyl)phenyl
946	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
947	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
948	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
949	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
950	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
951	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
952	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-5-yl)furanyl
953	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-6-yl)thienyl
954	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-tetrazolylphenyl)phenyl

Tabl 16

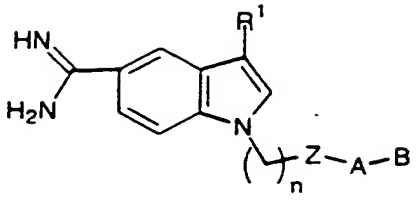


Ex	n	Z	A-B
1001	1	C(O)	4-(2-aminosulfonylphenyl)phenyl
1002	1	C(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
1003	1	C(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
1004	1	C(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1005	1	C(O)	2-aminosulfonyl-4-cyclohexylphenyl
1006	1	C(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
1007	1	C(O)	2-(5-indazol-5-yl)furanyl
1008	1	C(O)	2-(5-indazol-6-yl)thienyl
1009	1	C(O)	4-(2-tetrazolylphenyl)phenyl
1010	1	C(O)NH	4-(2-aminosulfonylphenyl)phenyl
1011	1	C(O)NH	4-(2-aminosulfonylphenyl)-2-pyridyl
1012	1	C(O)NH	4-(2-methylaminosulfonyl-phenyl)phenyl
1013	1	C(O)NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1014	1	C(O)NH	2-aminosulfonyl-4-cyclohexylphenyl
1015	1	C(O)NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
1016	1	C(O)NH	2-(5-indazol-5-yl)furanyl
1017	1	C(O)NH	2-(5-indazol-6-yl)thienyl

1018	1	C(O)NH	4-(2-tetrazolylphenyl)phenyl
1019	1	NHC(O)	4-(2-aminosulfonylphenyl)phenyl
1020	1	NHC(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
1021	1	NHC(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
1022	1	NHC(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1023	1	NHC(O)	2-aminosulfonyl-4-cyclohexylphenyl
1024	1	NHC(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
1025	1	NHC(O)	2-(5-indazol-5-yl)furanyl
1026	1	NHC(O)	2-(5-indazol-6-yl)thienyl
1027	1	NHC(O)	4-(2-tetrazolylphenyl)phenyl
1028	1	SO_2NH	4-(2-aminosulfonylphenyl)phenyl
1029	1	SO_2NH	4-(2-aminosulfonylphenyl)-2-pyridyl
1030	1	SO_2NH	4-(2-methylaminosulfonyl-phenyl)phenyl
1031	1	SO_2NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1032	1	SO_2NH	2-aminosulfonyl-4-cyclohexylphenyl
1033	1	SO_2NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
1034	1	SO_2NH	2-(5-indazol-5-yl)furanyl
1035	1	SO_2NH	2-(5-indazol-6-yl)thienyl
1036	1	SO_2NH	4-(2-tetrazolylphenyl)phenyl
1037	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
1038	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl

1039	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
1040	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1041	0	$CH(CH_2CH_2OH)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
1042	0	$CH(CH_2CH_2OH)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
1043	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-5-yl)furanyl
1044	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-6-yl)thienyl
1045	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-tetrazolylphenyl)phenyl
1046	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
1047	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
1048	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
1049	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1050	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
1051	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
1052	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-5-yl)furanyl
1053	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-6-yl)thienyl
1054	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-tetrazolylphenyl)phenyl

Table 17



Ex	n	Z	R^1	A-B
1101	1	C(O)	H	3-acetyl-4-benzylpiperidine
1102	1	C(O)	H	4-(4-fluorobenzyl)piperidine
1103	1	C(O)	H	4-(2,3-difluorobenzyl) piperidine
1104	1	C(O)	H	4-(2-chloro-4-fluorobenzyl) piperidine
1105	1	C(O)	CH_2CH_2OH	3-acetyl-4-benzylpiperidine
1106	1	C(O)	CH_2CH_2OH	4-(3-fluorobenzyl)piperidine
1107	1	C(O)	CH_2CH_2OH	4-(4-fluorobenzyl)piperidine
1108	1	C(O)	CH_2CH_2OH	4-(2,3-difluorobenzyl) piperidine
1109	1	C(O)	CH_2CH_2OH	4-(2-chloro-4-fluorobenzyl) piperidine
1110	1	C(O)	CH_2OCH_3	4-benzylpiperidine
1111	1	C(O)	CH_2OCH_3	3-acetyl-4-benzylpiperidine
1112	1	C(O)	CH_2OCH_3	4-(3-fluorobenzyl)piperidine
1113	1	C(O)	CH_2OCH_3	4-(4-fluorobenzyl)piperidine
1114	1	C(O)	CH_2OCH_3	4-(2,3-difluorobenzyl) piperidine
1115	1	C(O)	CH_2OCH_3	4-(2-chloro-4-fluorobenzyl) piperidine
1116	1	C(O)	CH_2CH_2-tetrazolyl	4-benzylpiperidine
1117	1	C(O)	CH_2CH_2-tetrazolyl	3-acetyl-4-benzylpiperidine
1118	1	C(O)	CH_2CH_2-tetrazolyl	4-(3-fluorobenzyl)piperidine

1119	1	C(O)	CH_2CH_2-tetrazolyl	4-(4-fluorobenzyl)piperidine
1120	1	C(O)	CH_2CH_2-tetrazolyl	4-(2,3-difluorobenzyl) piperidine
1121	1	C(O)	CH_2CH_2-tetrazolyl	4-(2-chloro-4-fluorobenzyl) piperidine
1122	1	C(O)NH	H	3-acetyl-4-benzylpiperidine
1123	1	C(O)NH	H	4-(3-fluorobenzyl)piperidine
1124	1	C(O)NH	H	4-(4-fluorobenzyl)piperidine
1125	1	C(O)NH	H	4-(2,3-difluorobenzyl) piperidine
1126	1	C(O)NH	H	4-(2-chloro-4-fluorobenzyl) piperidine
1127	1	C(O)NH	CH_2CH_2OH	4-benzylpiperidine
1128	1	C(O)NH	CH_2CH_2OH	3-acetyl-4-benzylpiperidine
1129	1	C(O)NH	CH_2CH_2OH	4-(3-fluorobenzyl)piperidine
1130	1	C(O)NH	CH_2CH_2OH	4-(4-fluorobenzyl)piperidine
1131	1	C(O)NH	CH_2CH_2OH	4-(2,3-difluorobenzyl) piperidine
1132	1	C(O)NH	CH_2CH_2OH	4-(2-chloro-4-fluorobenzyl) piperidine
1133	1	C(O)NH	CH_2OCH_3	4-benzylpiperidine
1134	1	C(O)NH	CH_2OCH_3	3-acetyl-4-benzylpiperidine
1135	1	C(O)NH	CH_2OCH_3	4-(3-fluorobenzyl)piperidine
1136	1	C(O)NH	CH_2OCH_3	4-(4-fluorobenzyl)piperidine
1137	1	C(O)NH	CH_2OCH_3	4-(2,3-difluorobenzyl) piperidine
1138	1	C(O)NH	CH_2OCH_3	4-(2-chloro-4-fluorobenzyl) piperidine
1139	1	C(O)NH	CH_2CH_2-tetrazolyl	4-benzylpiperidine
1140	1	C(O)NH	CH_2CH_2-tetrazolyl	3-acetyl-4-benzylpiperidine
1141	1	C(O)NH	CH_2CH_2-tetrazolyl	4-(3-fluorobenzyl)piperidine

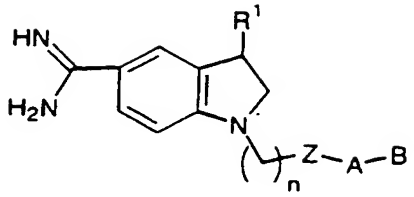
1142	1	C(O)NH	CH_2CH_2-tetrazolyl	4-(4-fluorobenzyl)piperidine
1143	1	C(O)NH	CH_2CH_2-tetrazolyl	4-(2,3-difluorobenzyl) piperidine
1144	1	C(O)NH	CH_2CH_2-tetrazolyl	4-(2-chloro-4-fluorobenzyl) piperidine
1145	1	SO_2NH	H	4-benzylpiperidine
1146	1	SO_2NH	H	3-acetyl-4-benzylpiperidine
1147	1	SO_2NH	H	4-(3-fluorobenzyl)piperidine
1148	1	SO_2NH	H	4-(4-fluorobenzyl)piperidine
1149	1	SO_2NH	H	4-(2,3-difluorobenzyl) piperidine
1150	1	SO_2NH	H	4-(2-chloro-4-fluorobenzyl) piperidine
1151	1	SO_2NH	CH_2CH_2OH	4-benzylpiperidine
1152	1	SO_2NH	CH_2CH_2OH	3-acetyl-4-benzylpiperidine
1153	1	SO_2NH	CH_2CH_2OH	4-(3-fluorobenzyl)piperidine
1154	1	SO_2NH	CH_2CH_2OH	4-(4-fluorobenzyl)piperidine
1155	1	SO_2NH	CH_2CH_2OH	4-(2,3-difluorobenzyl) piperidine
1156	1	SO_2NH	CH_2CH_2OH	4-(2-chloro-4-fluorobenzyl) piperidine
1157	1	SO_2NH	CH_2OCH_3	4-benzylpiperidine
1158	1	SO_2NH	CH_2OCH_3	3-acetyl-4-benzylpiperidine
1159	1	SO_2NH	CH_2OCH_3	4-(3-fluorobenzyl)piperidine
1160	1	SO_2NH	CH_2OCH_3	4-(4-fluorobenzyl)piperidine
1161	1	SO_2NH	CH_2OCH_3	4-(2,3-difluorobenzyl) piperidine
1162	1	SO_2NH	CH_2OCH_3	4-(2-chloro-4-fluorobenzyl) piperidine
1163	1	SO_2NH	CH_2CH_2-tetrazolyl	4-benzylpiperidine
1164	1	SO_2NH	CH_2CH_2-tetrazolyl	3-acetyl-4-benzylpiperidine
1165	1	SO_2NH	CH_2CH_2-tetrazolyl	4-(3-fluorobenzyl)piperidine

1166	1	SO_2NH	CH_2CH_2-tetrazolyl	4-(4-fluorobenzyl)piperidine
1167	1	SO_2NH	CH_2CH_2-tetrazolyl	4-(2,3-difluorobenzyl) piperidine
1168	1	SO_2NH	CH_2CH_2-tetrazolyl	4-(2-chloro-4-fluorobenzyl) piperidine

1245	1	C(O)NH	CH_2CH_2-tetrazolyl	4-(3-fluorobenzyl)piperidine
1246	1	C(O)NH	CH_2CH_2-tetrazolyl	4-(4-fluorobenzyl)piperidine
1247	1	C(O)NH	CH_2CH_2-tetrazolyl	4-(2,3-difluorobenzyl) piperidine
1248	1	C(O)NH	CH_2CH_2-tetrazolyl	4-(2-chloro-4-fluorobenzyl) piperidine
1249	1	SO_2NH	H	4-benzylpiperidine
1250	1	SO_2NH	H	3-acetyl-4-benzylpiperidine
1251	1	SO_2NH	H	4-(3-fluorobenzyl)piperidine
1252	1	SO_2NH	H	4-(4-fluorobenzyl)piperidine
1253	1	SO_2NH	H	4-(2,3-difluorobenzyl) piperidine
1254	1	SO_2NH	H	4-(2-chloro-4-fluorobenzyl) piperidine
1255	1	SO_2NH	CH_2CH_2OH	4-benzylpiperidine
1256	1	SO_2NH	CH_2CH_2OH	3-acetyl-4-benzylpiperidine
1257	1	SO_2NH	CH_2CH_2OH	4-(3-fluorobenzyl)piperidine
1258	1	SO_2NH	CH_2CH_2OH	4-(4-fluorobenzyl)piperidine
1259	1	SO_2NH	CH_2CH_2OH	4-(2,3-difluorobenzyl) piperidine
1260	1	SO_2NH	CH_2CH_2OH	4-(2-chloro-4-fluorobenzyl) piperidine
1261	1	SO_2NH	CH_2OCH_3	4-benzylpiperidine
1262	1	SO_2NH	CH_2OCH_3	3-acetyl-4-benzylpiperidine
1263	1	SO_2NH	CH_2OCH_3	4-(3-fluorobenzyl)piperidine
1264	1	SO_2NH	CH_2OCH_3	4-(4-fluorobenzyl)piperidine
1265	1	SO_2NH	CH_2OCH_3	4-(2,3-difluorobenzyl) piperidine
1266	1	SO_2NH	CH_2OCH_3	4-(2-chloro-4-fluorobenzyl) piperidine
1267	1	SO_2NH	CH_2CH_2-tetrazolyl	4-benzylpiperidine
1268	1	SO_2NH	CH_2CH_2-tetrazolyl	3-acetyl-4-benzylpiperidine

1269	1	SO_2NH	CH_2CH_2-tetrazolyl	4-(3-fluorobenzyl)piperidine
1270	1	SO_2NH	CH_2CH_2-tetrazolyl	4-(4-fluorobenzyl)piperidine
1271	1	SO_2NH	CH_2CH_2-tetrazolyl	4-(2,3-difluorobenzyl) piperidine
1272	1	SO_2NH	CH_2CH_2-tetrazolyl	4-(2-chloro-4-fluorobenzyl) piperidine

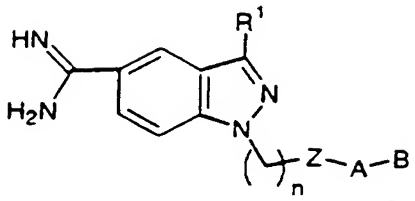
Table 18



Ex	n	Z	R^1	A-B
1201	1	C(O)	H	4-benzylpiperidine
1202	1	C(O)	H	3-acetyl-4-benzylpiperidine
1203	1	C(O)	H	4-(3-fluorobenzyl)piperidine
1204	1	C(O)	H	4-(4-fluorobenzyl)piperidine
1205	1	C(O)	H	4-(2,3-difluorobenzyl) piperidine
1206	1	C(O)	H	4-(2-chloro-4-fluorobenzyl) piperidine
1207	1	C(O)	CH_2CH_2OH	4-benzylpiperidine
1208	1	C(O)	CH_2CH_2OH	3-acetyl-4-benzylpiperidine
1209	1	C(O)	CH_2CH_2OH	4-(3-fluorobenzyl)piperidine
1210	1	C(O)	CH_2CH_2OH	4-(4-fluorobenzyl)piperidine
1211	1	C(O)	CH_2CH_2OH	4-(2,3-difluorobenzyl) piperidine
1212	1	C(O)	CH_2CH_2OH	4-(2-chloro-4-fluorobenzyl) piperidine
1213	1	C(O)	CH_2OCH_3	4-benzylpiperidine
1214	1	C(O)	CH_2OCH_3	3-acetyl-4-benzylpiperidine
1215	1	C(O)	CH_2OCH_3	4-(3-fluorobenzyl)piperidine
1216	1	C(O)	CH_2OCH_3	4-(4-fluorobenzyl)piperidine
1217	1	C(O)	CH_2OCH_3	4-(2,3-difluorobenzyl) piperidine
1218	1	C(O)	CH_2OCH_3	4-(2-chloro-4-fluorobenzyl) piperidine
1219	1	C(O)	CH_2CH_2-tetrazolyl	4-benzylpiperidine
1220	1	C(O)	CH_2CH_2-tetrazolyl	3-acetyl-4-benzylpiperidine

1221	1	C(O)	CH_2CH_2-tetrazolyl	4-(3-fluorobenzyl)piperidine
1222	1	C(O)	CH_2CH_2-tetrazolyl	4-(4-fluorobenzyl)piperidine
1223	1	C(O)	CH_2CH_2-tetrazolyl	4-(2,3-difluorobenzyl) piperidine
1224	1	C(O)	CH_2CH_2-tetrazolyl	4-(2-chloro-4-fluorobenzyl) piperidine
1225	1	C(O)NH	H	4-benzylpiperidine
1226	1	C(O)NH	H	3-acetyl-4-benzylpiperidine
1227	1	C(O)NH	H	4-(3-fluorobenzyl)piperidine
1228	1	C(O)NH	H	4-(4-fluorobenzyl)piperidine
1229	1	C(O)NH	H	4-(2,3-difluorobenzyl) piperidine
1230	1	C(O)NH	H	4-(2-chloro-4-fluorobenzyl) piperidine
1231	1	C(O)NH	CH_2CH_2OH	4-benzylpiperidine
1232	1	C(O)NH	CH_2CH_2OH	3-acetyl-4-benzylpiperidine
1233	1	C(O)NH	CH_2CH_2OH	4-(3-fluorobenzyl)piperidine
1234	1	C(O)NH	CH_2CH_2OH	4-(4-fluorobenzyl)piperidine
1235	1	C(O)NH	CH_2CH_2OH	4-(2,3-difluorobenzyl) piperidine
1236	1	C(O)NH	CH_2CH_2OH	4-(2-chloro-4-fluorobenzyl) piperidine
1237	1	C(O)NH	CH_2OCH_3	4-benzylpiperidine
1238	1	C(O)NH	CH_2OCH_3	3-acetyl-4-benzylpiperidine
1239	1	C(O)NH	CH_2OCH_3	4-(3-fluorobenzyl)piperidine
1240	1	C(O)NH	CH_2OCH_3	4-(4-fluorobenzyl)piperidine
1241	1	C(O)NH	CH_2OCH_3	4-(2,3-difluorobenzyl) piperidine
1242	1	C(O)NH	CH_2OCH_3	4-(2-chloro-4-fluorobenzyl) piperidine
1243	1	C(O)NH	CH_2CH_2-tetrazolyl	4-benzylpiperidine
1244	1	C(O)NH	CH_2CH_2-tetrazolyl	3-acetyl-4-benzylpiperidine

Table 19



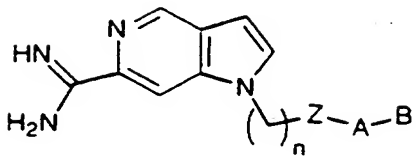
Ex	n	Z	R^1	A-B
1301	1	C(O)	H	4-benzylpiperidine
1302	1	C(O)	H	3-acetyl-4-benzylpiperidine
1303	1	C(O)	H	4-(3-fluorobenzyl)piperidine
1304	1	C(O)	H	4-(4-fluorobenzyl)piperidine
1305	1	C(O)	H	4-(2,3-difluorobenzyl) piperidine
1306	1	C(O)	H	4-(2-chloro-4-fluorobenzyl) piperidine
1307	1	C(O)	CH_2CH_2OH	4-benzylpiperidine
1308	1	C(O)	CH_2CH_2OH	3-acetyl-4-benzylpiperidine
1309	1	C(O)	CH_2CH_2OH	4-(3-fluorobenzyl)piperidine
1310	1	C(O)	CH_2CH_2OH	4-(4-fluorobenzyl)piperidine
1311	1	C(O)	CH_2CH_2OH	4-(2,3-difluorobenzyl) piperidine
1312	1	C(O)	CH_2CH_2OH	4-(2-chloro-4-fluorobenzyl) piperidine
1313	1	C(O)	CH_2OCH_3	4-benzylpiperidine
1314	1	C(O)	CH_2OCH_3	3-acetyl-4-benzylpiperidine
1315	1	C(O)	CH_2OCH_3	4-(3-fluorobenzyl)piperidine
1316	1	C(O)	CH_2OCH_3	4-(4-fluorobenzyl)piperidine
1317	1	C(O)	CH_2OCH_3	4-(2,3-difluorobenzyl) piperidine
1318	1	C(O)	CH_2OCH_3	4-(2-chloro-4-fluorobenzyl) piperidine
1319	1	C(O)	CH_2CH_2-tetrazolyl	4-benzylpiperidine
1320	1	C(O)	CH_2CH_2-tetrazolyl	3-acetyl-4-benzylpiperidine

1321	1	C(O)	CH_2CH_2-tetrazolyl	4-(3-fluorobenzyl)piperidine
1322	1	C(O)	CH_2CH_2-tetrazolyl	4-(4-fluorobenzyl)piperidine
1323	1	C(O)	CH_2CH_2-tetrazolyl	4-(2,3-difluorobenzyl) piperidine
1324	1	C(O)	CH_2CH_2-tetrazolyl	4-(2-chloro-4-fluorobenzyl) piperidine
1325	1	C(O)NH	H	4-benzylpiperidine
1326	1	C(O)NH	H	3-acetyl-4-benzylpiperidine
1327	1	C(O)NH	H	4-(3-fluorobenzyl)piperidine
1328	1	C(O)NH	H	4-(4-fluorobenzyl)piperidine
1329	1	C(O)NH	H	4-(2,3-difluorobenzyl) piperidine
1330	1	C(O)NH	H	4-(2-chloro-4-fluorobenzyl) piperidine
1331	1	C(O)NH	CH_2CH_2OH	4-benzylpiperidine
1332	1	C(O)NH	CH_2CH_2OH	3-acetyl-4-benzylpiperidine
1333	1	C(O)NH	CH_2CH_2OH	4-(3-fluorobenzyl)piperidine
1334	1	C(O)NH	CH_2CH_2OH	4-(4-fluorobenzyl)piperidine
1335	1	C(O)NH	CH_2CH_2OH	4-(2,3-difluorobenzyl) piperidine
1336	1	C(O)NH	CH_2CH_2OH	4-(2-chloro-4-fluorobenzyl) piperidine
1337	1	C(O)NH	CH_2OCH_3	4-benzylpiperidine
1338	1	C(O)NH	CH_2OCH_3	3-acetyl-4-benzylpiperidine
1339	1	C(O)NH	CH_2OCH_3	4-(3-fluorobenzyl)piperidine
1340	1	C(O)NH	CH_2OCH_3	4-(4-fluorobenzyl)piperidine
1341	1	C(O)NH	CH_2OCH_3	4-(2,3-difluorobenzyl) piperidine
1342	1	C(O)NH	CH_2OCH_3	4-(2-chloro-4-fluorobenzyl) piperidine
1343	1	C(O)NH	CH_2CH_2-tetrazolyl	4-benzylpiperidine
1344	1	C(O)NH	CH_2CH_2-tetrazolyl	3-acetyl-4-benzylpiperidine

1345	1	C(O)NH	CH_2CH_2-tetrazolyl	4-(3-fluorobenzyl)piperidine
1346	1	C(O)NH	CH_2CH_2-tetrazolyl	4-(4-fluorobenzyl)piperidine
1347	1	C(O)NH	CH_2CH_2-tetrazolyl	4-(2,3-difluorobenzyl) piperidine
1348	1	C(O)NH	CH_2CH_2-tetrazolyl	4-(2-chloro-4-fluorobenzyl) piperidine
1349	1	SO_2NH	H	4-benzylpiperidine
1350	1	SO_2NH	H	3-acetyl-4-benzylpiperidine
1351	1	SO_2NH	H	4-(3-fluorobenzyl)piperidine
1352	1	SO_2NH	H	4-(4-fluorobenzyl)piperidine
1353	1	SO_2NH	H	4-(2,3-difluorobenzyl) piperidine
1354	1	SO_2NH	H	4-(2-chloro-4-fluorobenzyl) piperidine
1355	1	SO_2NH	CH_2CH_2OH	4-benzylpiperidine
1356	1	SO_2NH	CH_2CH_2OH	3-acetyl-4-benzylpiperidine
1357	1	SO_2NH	CH_2CH_2OH	4-(3-fluorobenzyl)piperidine
1358	1	SO_2NH	CH_2CH_2OH	4-(4-fluorobenzyl)piperidine
1359	1	SO_2NH	CH_2CH_2OH	4-(2,3-difluorobenzyl) piperidine
1360	1	SO_2NH	CH_2CH_2OH	4-(2-chloro-4-fluorobenzyl) piperidine
1361	1	SO_2NH	CH_2OCH_3	4-benzylpiperidine
1362	1	SO_2NH	CH_2OCH_3	3-acetyl-4-benzylpiperidine
1363	1	SO_2NH	CH_2OCH_3	4-(3-fluorobenzyl)piperidine
1364	1	SO_2NH	CH_2OCH_3	4-(4-fluorobenzyl)piperidine
1365	1	SO_2NH	CH_2OCH_3	4-(2,3-difluorobenzyl) piperidine
1366	1	SO_2NH	CH_2OCH_3	4-(2-chloro-4-fluorobenzyl) piperidine
1367	1	SO_2NH	CH_2CH_2-tetrazolyl	4-benzylpiperidine
1368	1	SO_2NH	CH_2CH_2-tetrazolyl	3-acetyl-4-benzylpiperidine

1369	1	SO_2NH	CH_2CH_2-tetrazolyl	4-(3-fluorobenzyl)piperidine
1370	1	SO_2NH	CH_2CH_2-tetrazolyl	4-(4-fluorobenzyl)piperidine
1371	1	SO_2NH	CH_2CH_2-tetrazolyl	4-(2,3-difluorobenzyl) piperidine
1372	1	SO_2NH	CH_2CH_2-tetrazolyl	4-(2-chloro-4-fluorobenzyl) piperidine

Table 20

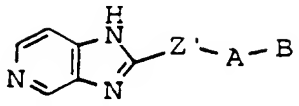


Ex	n	Z	A-B
1401	1	C(O)	4-(2-aminosulfonylphenyl)phenyl
1402	1	C(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
1403	1	C(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
1404	1	C(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1405	1	C(O)	2-aminosulfonyl-4-cyclohexylphenyl
1406	1	C(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
1407	1	C(O)	2-(5-indazol-5-yl)furanyl
1408	1	C(O)	2-(5-indazol-6-yl)thienyl
1409	1	C(O)	4-(2-tetrazolylphenyl)phenyl
1410	1	C(O)NH	4-(2-aminosulfonylphenyl)phenyl
1411	1	C(O)NH	4-(2-aminosulfonylphenyl)-2-pyridyl
1412	1	C(O)NH	4-(2-methylaminosulfonyl-phenyl)phenyl
1413	1	C(O)NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1414	1	C(O)NH	2-aminosulfonyl-4-cyclohexylphenyl
1415	1	C(O)NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
1416	1	C(O)NH	2-(5-indazol-5-yl)furanyl
1417	1	C(O)NH	2-(5-indazol-6-yl)thienyl

1418	1	C(O)NH	4-(2-tetrazolylphenyl)phenyl
1419	1	NHC(O)	4-(2-aminosulfonylphenyl)phenyl
1420	1	NHC(O)	4-(2-aminosulfonylphenyl)-2-pyridyl
1421	1	NHC(O)	4-(2-methylaminosulfonyl-phenyl)phenyl
1422	1	NHC(O)	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1423	1	NHC(O)	2-aminosulfonyl-4-cyclohexylphenyl
1424	1	NHC(O)	3-aminosulfonyl-4-t-butyl-2-pyridyl
1425	1	NHC(O)	2-(5-indazol-5-yl)furanyl
1426	1	NHC(O)	2-(5-indazol-6-yl)thienyl
1427	1	NHC(O)	4-(2-tetrazolylphenyl)phenyl
1428	1	SO_2NH	4-(2-aminosulfonylphenyl)phenyl
1429	1	SO_2NH	4-(2-aminosulfonylphenyl)-2-pyridyl
1430	1	SO_2NH	4-(2-methylaminosulfonyl-phenyl)phenyl
1431	1	SO_2NH	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1432	1	SO_2NH	2-aminosulfonyl-4-cyclohexylphenyl
1433	1	SO_2NH	3-aminosulfonyl-4-t-butyl-2-pyridyl
1434	1	SO_2NH	2-(5-indazol-5-yl)furanyl
1435	1	SO_2NH	2-(5-indazol-6-yl)thienyl
1436	1	SO_2NH	4-(2-tetrazolylphenyl)phenyl
1437	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
1438	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl

1439	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
1440	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1441	0	$CH(CH_2CH_2OH)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
1442	0	$CH(CH_2CH_2OH)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
1443	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-5-yl)furanyl
1444	0	$CH(CH_2CH_2OH)C(O)NH$	2-(5-indazol-6-yl)thienyl
1445	0	$CH(CH_2CH_2OH)C(O)NH$	4-(2-tetrazolylphenyl)phenyl
1446	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
1447	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
1448	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
1449	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1450	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
1451	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
1452	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-5-yl)furanyl
1453	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	2-(5-indazol-6-yl)thienyl
1454	0	$CH(CH_2$-tetrazolyl$)C(O)NH$	4-(2-tetrazolylphenyl)phenyl

Tabl 21



Ex	Z'	A-B
1501	$CH_2C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
1502	$CH_2C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
1503	$CH_2C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
1504	$CH_2C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1505	$CH_2C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
1506	$CH_2C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
1507	$CH_2C(O)NH$	2-(5-indazol-5-yl)furanyl
1508	$CH_2C(O)NH$	2-(5-indazol-6-yl)thienyl
1509	$CH_2C(O)NH$	4-(2-tetrazolylphenyl)phenyl
1510	$CH_2CH_2C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
1511	$CH_2CH_2C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
1512	$CH_2CH_2C(O)NH$	4-(2-tert-butylaminosulfonyl-phenyl)phenyl
1513	$CH_2CH_2C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1514	$CH_2CH_2C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
1515	$CH_2CH_2C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
1516	$CH_2CH_2C(O)NH$	2-(5-indazol-5-yl)furanyl
1517	$CH_2CH_2C(O)NH$	2-(5-indazol-6-yl)thienyl
1518	$CH_2CH_2C(O)NH$	4-(2-tetrazolylphenyl)phenyl

1519	$SCH_2C(O)NH$	4-(2-aminosulfonylphenyl)phenyl
1520	$SCH_2C(O)NH$	4-(2-aminosulfonylphenyl)-2-pyridyl
1521	$SCH_2C(O)NH$	4-(2-methylaminosulfonyl-phenyl)phenyl
1522	$SCH_2C(O)NH$	4-(2-ethylaminosulfonyl-phenyl)-2-pyridyl
1523	$SCH_2C(O)NH$	2-aminosulfonyl-4-cyclohexylphenyl
1524	$SCH_2C(O)NH$	3-aminosulfonyl-4-t-butyl-2-pyridyl
1525	$SCH_2C(O)NH$	2-(5-indazol-5-yl)furanyl
1526	$SCH_2C(O)NH$	2-(5-indazol-6-yl)thienyl
1527	$SCH_2C(O)NH$	4-(2-tetrazolylphenyl)phenyl

Utility

The compounds of this invention are useful as anticoagulants for the treatment or prevention of thromboembolic disorders in mammals. The term "thromboembolic disorders" as used herein includes arterial or venous cardiovascular or cerebrovascular thromboembolic disorders, including, for example, unstable angina, first or recurrent myocardial infarction, ischemic sudden death, transient ischemic attack, stroke, atherosclerosis, venous thrombosis, deep vein thrombosis, thrombophlebitis, arterial embolism, coronary and cerebral arterial thrombosis, cerebral embolism, kidney embolisms, and pulmonary embolisms. The anticoagulant effect of compounds of the present invention is believed to be due to inhibition of factor Xa or thrombin.

The effectiveness of compounds of the present invention as inhibitors of factor Xa was determined using purified human factor Xa and synthetic substrate. The rate of factor Xa hydrolysis of chromogenic substrate S2222 (Kabi Pharmacia, Franklin, OH) was measured both in the absence and presence of compounds of the present invention. Hydrolysis of the substrate resulted in the release of pNA, which was monitored spectrophotometrically by measuring the increase in absorbance at 405 nM. A decrease in the rate of absorbance change at 405 nm in the presence of inhibitor is indicative of enzyme inhibition. The results of this assay are expressed as inhibitory constant, K_i.

Factor Xa determinations were made in 0.10 M sodium phosphate buffer, pH 7.5, containing 0.20 M NaCl, and 0.5 % PEG 8000. The Michaelis constant, K_m, for substrate hydrolysis was determined at 25°C using the method of Lineweaver and Burk. Values of K_i were determined by allowing 0.2-0.5 nM human factor Xa (Enzyme Research Laboratories, South Bend, IN) to react with the substrate (0.20 mM-1 mM) in the presence of inhibitor. Reactions were allowed to go for 30 minutes and the velocities (rate of absorbance change vs time) were measured in the time frame of 25-30 minutes. The following relationship was used to calculate K_i values:

$$(v_o - v_s)/v_s = I/(K_i\ (1 + S/K_m))$$

where:

v_o is the velocity of the control in the absence of inhibitor;

v_s is the velocity in the presence of inhibitor;

I is the concentration of inhibitor;

K_i is the dissociation constant of the enzyme:inhibitor complex;

S is the concentration of substrate;

K_m is the Michaelis constant.

Using the methodology described above, a number of compounds of the present invention were found to exhibit a K_i of ≤ 5 μm, thereby confirming the utility of the compounds of the present invention as effective Xa inhibitors.

The antithrombotic effect of compounds of the present invention can be demonstrated in a rabbit arterio-venous (AV) shunt thrombosis model. In this model, rabbits weighing 2-3 kg anesthetized with a mixture of xylazine (10 mg/kg i.m.) and ketamine (50 mg/kg i.m.) are used. A saline-filled AV shunt device is connected between the femoral arterial and the femoral venous cannulae. The AV shunt device consists of a piece of 6-cm tygon tubing which contains a piece of silk thread. Blood will flow from the femoral artery via the AV-shunt into the femoral vein. The exposure of flowing blood to a silk thread will induce the formation of a significant thrombus. After forty minutes, the shunt is disconnected and the silk thread covered with thrombus is weighed. Test agents or vehicle will be given (i.v., i.p., s.c., or orally) prior to the opening of the AV shunt. The percentage inhibition of thrombus formation is determined for each treatment group. The ID50 values (dose which produces 50% inhibition of thrombus formation) are estimated by linear regression.

The compounds of formula (I) are also considered to be useful as inhibitors of serine proteases, notably human thrombin, plasma kallikrein and plasmin. Because of their inhibitory action, these compounds are indicated for use in the prevention or treatment of physiological reactions, blood coagulation and inflammation, catalyzed by the aforesaid class of enzymes. Specifically, the compounds have utility as drugs

for the treatment of diseases arising from elevated thrombin activity such as myocardial infarction, and as reagents used as anticoagulants in the processing of blood to plasma for diagnostic and other commercial purposes.

Some compounds of the present invention were shown to be direct acting inhibitors of the serine protease thrombin by their ability to inhibit the cleavage of small molecule substrates by thrombin in a purified system. *In vitro* inhibition constants were determined by the method described by Kettner et al. in *J. Biol. Chem.* **265**, 18289-18297 (1990), herein incorporated by reference. In these assays, thrombin-mediated hydrolysis of the chromogenic substrate S2238 (Helena Laboratories, Beaumont, TX) was monitored spectrophotometrically. Addition of an inhibitor to the assay mixture results in decreased absorbance and is indicative of thrombin inhibition. Human thrombin (Enzyme Research Laboratories, Inc., South Bend, IN) at a concentration of 0.2 nM in 0.10 M sodium phosphate buffer, pH 7.5, 0.20 M NaCl, and 0.5% PEG 6000, was incubated with various substrate concentrations ranging from 0.20 to 0.02 mM. After 25 to 30 minutes of incubation, thrombin activity was assayed by monitoring the rate of increase in absorbance at 405 nm which arises owing to substrate hydrolysis. Inhibition constants were derived from reciprocal plots of the reaction velocity as a function of substrate concentration using the standard method of Lineweaver and Burk. Using the methodology described above, some compounds of this invention were evaluated and found to exhibit a K_i of less than 5 μm, thereby confirming the utility of the compounds of the invention as effective thrombin inhibitors.

The compounds of the present invention can be administered alone or in combination with one or more additional therapeutic agents. These include other anti-coagulant or coagulation inhibitory agents, anti-platelet or platelet inhibitory agents, thrombin inhibitors, or thrombolytic or fibrinolytic agents.

The compounds are administered to a mammal in a therapeutically effective amount. By "therapeutically

effective amount" it is meant an amount of a compound of Formula I that, when administered alone or in combination with an additional therapeutic agent to a mammal, is effective to prevent or ameliorate the thromboembolic disease condition or the progression of the disease.

By "administered in combination" or "combination therapy" it is meant that the compound of Formula I and one or more additional therapeutic agents are administered concurrently to the mammal being treated. When administered in combination each component may be administered at the same time or sequentially in any order at different points in time. Thus, each component may be administered separately but sufficiently closely in time so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in combination with the compounds of this invention include warfarin and heparin, as well as other factor Xa inhibitors such as those described in the publications identified above under Background of the Invention.

The term anti-platelet agents (or platelet inhibitory agents), as used herein, denotes agents that inhibit platelet function such as by inhibiting the aggregation, adhesion or granular secretion of platelets. Such agents include, but are not limited to, the various known non-steroidal anti-inflammatory drugs (NSAIDS) such as aspirin, ibuprofen, naproxen, sulindac, indomethacin, mefenamate, droxicam, diclofenac, sulfinpyrazone, and piroxicam, including pharmaceutically acceptable salts or prodrugs thereof. Of the NSAIDS, aspirin (acetylsalicyclic acid or ASA), and piroxicam are preferred. Other suitable anti-platelet agents include ticlopidine, including pharmaceutically acceptable salts or prodrugs thereof. Ticlopidine is also a preferred compound since it is known to be gentle on the gastro-intestinal tract in use. Still other suitable platelet inhibitory agents include IIb/IIIa antagonists, thromboxane-A2-receptor antagonists and thromboxane-A2-synthetase inhibitors, as well as pharmaceutically acceptable salts or prodrugs thereof.

The term thrombin inhibitors (or anti-thrombin agents), as used herein, denotes inhibitors of the serine protease thrombin. By inhibiting thrombin, various thrombin-mediated processes, such as thrombin-mediated platelet activation (that is, for example, the aggregation of platelets, and/or the granular secretion of plasminogen activator inhibitor-1 and/or serotonin) and/or fibrin formation are disrupted. A number of thrombin inhibitors are known to one of skill in the art and these inhibitors are contemplated to be used in combination with the present compounds. Such inhibitors include, but are not limited to, boroarginine derivatives, boropeptides, heparins, hirudin and argatroban, including pharmaceutically acceptable salts and prodrugs thereof. Boroarginine derivatives and boropeptides include N-acetyl and peptide derivatives of boronic acid, such as C-terminal a-aminoboronic acid derivatives of lysine, ornithine, arginine, homoarginine and corresponding isothiouronium analogs thereof. The term hirudin, as used herein, includes suitable derivatives or analogs of hirudin, referred to herein as hirulogs, such as disulfatohirudin. Boropeptide thrombin inhibitors include compounds described in Kettner et al., U.S. Patent No. 5,187,157 and European Patent Application Publication Number 293 881 A2, the disclosures of which are hereby incorporated herein by reference. Other suitable boroarginine derivatives and boropeptide thrombin inhibitors include those disclosed in PCT Application Publication Number 92/07869 and European Patent Application Publication Number 471,651 A2, the disclosures of which are hereby incorporated herein by reference.

The term thrombolytics (or fibrinolytic) agents (or thrombolytics or fibrinolytics), as used herein, denotes agents that lyse blood clots (thrombi). Such agents include tissue plasminogen activator, anistreplase, urokinase or streptokinase, including pharmaceutically acceptable salts or prodrugs thereof. The term anistreplase, as used herein, refers to anisoylated plasminogen streptokinase activator complex, as described, for example, in European Patent Application No. 028,489, the disclosure of which is hereby

incorporated herein by reference herein. The term urokinase, as used herein, is intended to denote both dual and single chain urokinase, the latter also being referred to herein as prourokinase.

Administration of the compounds of Formula I of the invention in combination with such additional therapeutic agent, may afford an efficacy advantage over the compounds and agents alone, and may do so while permitting the use of lower doses of each. A lower dosage minimizes the potential of side effects, thereby providing an increased margin of safety.

The compounds of the present invention are also useful as standard or reference compounds, for example as a quality standard or control, in tests or assays involving the inhibition of factor Xa. Such compounds may be provided in a commercial kit, for example, for use in pharmaceutical research involving factor Xa. For example, a compound of the present invention could be used as a reference in an assay to compare its known activity to a compound with an unknown activity. This would ensure the experimenter that the assay was being performed properly and provide a basis for comparison, especially if the test compound was a derivative of the reference compound. When developing new assays or protocols, compounds according to the present invention could be used to test their effectiveness.

The compounds of the present invention may also be used in diagnostic assays involving factor Xa. For example, the presence of factor Xa in an unknown sample could be determined by addition of chromogenic substrate S2222 to a series of solutions containing test sample and optionally one of the compounds of the present invention. If production of pNA is observed in the solutions containing test sample, but no compound of the present invention, then one would conclude factor Xa was present.

Dosage and Formulation

The compounds of this invention can be administered in such oral dosage forms as tablets, capsules (each of which includes sustained release or timed release formulations),

pills, powders, granules, elixirs, tinctures, suspensions, syrups, and emulsions. They may also be administered in intravenous (bolus or infusion), intraperitoneal, subcutaneous, or intramuscular form, all using dosage forms well known to those of ordinary skill in the pharmaceutical arts. They can be administered alone, but generally will be administered with a pharmaceutical carrier selected on the basis of the chosen route of administration and standard pharmaceutical practice.

The dosage regimen for the compounds of the present invention will, of course, vary depending upon known factors, such as the pharmacodynamic characteristics of the particular agent and its mode and route of administration; the species, age, sex, health, medical condition, and weight of the recipient; the nature and extent of the symptoms; the kind of concurrent treatment; the frequency of treatment; the route of administration, the renal and hepatic function of the patient,and the effect desired. A physician or veterinarian can determine and prescribe the effective amount of the drug required to prevent, counter, or arrest the progress of the thromboembolic disorder.

By way of general guidance, the daily oral dosage of each active ingredient, when used for the indicated effects, will range between about 0.001 to 1000 mg/kg of body weight, preferably between about 0.01 to 100 mg/kg of body weight per day, and most preferably between about 1.0 to 20 mg/kg/day. Intravenously, the most preferred doses will range from about 1 to about 10 mg/kg/minute during a constant rate infusion. Compounds of this invention may be administered in a single daily dose, or the total daily dosage may be administered in divided doses of two, three, or four times daily.

Compounds of this invention can be administered in intranasal form via topical use of suitable intranasal vehicles, or via transdermal routes, using transdermal skin patches. When administered in the form of a transdermal delivery system, the dosage administration will, of course, be continuous rather than intermittent throughout the dosage regimen.

The compounds are typically administered in admixture with suitable pharmaceutical diluents, excipients, or carriers (collectively referred to herein as pharmaceutical carriers) suitably selected with respect to the intended form of administration, that is, oral tablets, capsules, elixirs, syrups and the like, and consistent with conventional pharmaceutical practices.

For instance, for oral administration in the form of a tablet or capsule, the active drug component can be combined with an oral, non-toxic, pharmaceutically acceptable, inert carrier such as lactose, starch, sucrose, glucose, methyl callulose, magnesium stearate, dicalcium phosphate, calcium sulfate, mannitol, sorbitol and the like; for oral administration in liquid form, the oral drug components can be combined with any oral, non-toxic, pharmaceutically acceptable inert carrier such as ethanol, glycerol, water, and the like. Moreover, when desired or necessary, suitable binders, lubricants, disintegrating agents, and coloring agents can also be incorporated into the mixture. Suitable binders include starch, gelatin, natural sugars such as glucose or beta-lactose, corn sweeteners, natural and synthetic gums such as acacia, tragacanth, or sodium alginate, carboxymethylcellulose, polyethylene glycol, waxes, and the like. Lubricants used in these dosage forms include sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride, and the like. Disintegrators include, without limitation, starch, methyl cellulose, agar, bentonite, xanthan gum, and the like.

The compounds of the present invention can also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar vesicles, and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, such as cholesterol, stearylamine, or phosphatidylcholines.

Compounds of the present invention may also be coupled with soluble polymers as targetable drug carriers. Such polymers can include polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamide-phenol,

polyhydroxyethylaspartamidephenol, or polyethyleneoxide-polylysine substituted with palmitoyl residues. Furthermore, the compounds of the present invention may be coupled to a class of biodegradable polymers useful in achieving controlled release of a drug, for example, polylactic acid, polyglycolic acid, copolymers of polylactic and polyglycolic acid, polyepsilon caprolactone, polyhydroxy butyric acid, polyorthoesters, polyacetals, polydihydropyrans, polycyanoacylates, and crosslinked or amphipathic block copolymers of hydrogels.

Dosage forms (pharmaceutical compositions) suitable for administration may contain from about 1 milligram to about 100 milligrams of active ingredient per dosage unit. In these pharmaceutical compositions the active ingredient will ordinarily be present in an amount of about 0.5-95% by weight based on the total weight of the composition.

Gelatin capsules may contain the active ingredient and powdered carriers, such as lactose, starch, cellulose derivatives, magnesium stearate, stearic acid, and the like. Similar diluents can be used to make compressed tablets. Both tablets and capsules can be manufactured as sustained release products to provide for continuous release of medication over a period of hours. Compressed tablets can be sugar coated or film coated to mask any unpleasant taste and protect the tablet from the atmosphere, or enteric coated for selective disintegration in the gastrointestinal tract.

Liquid dosage forms for oral administration can contain coloring and flavoring to increase patient acceptance.

In general, water, a suitable oil, saline, aqueous dextrose (glucose), and related sugar solutions and glycols such as propylene glycol or polyethylene glycols are suitable carriers for parenteral solutions. Solutions for parenteral administration preferably contain a water soluble salt of the active ingredient, suitable stabilizing agents, and if necessary, buffer substances. Antioxidizing agents such as sodium bisulfite, sodium sulfite, or ascorbic acid, either alone or combined, are suitable stabilizing agents. Also used are citric acid and its salts and sodium EDTA. In addition,

parenteral solutions can contain preservatives, such as benzalkonium chloride, methyl- or propyl-paraben, and chlorobutanol.

Suitable pharmaceutical carriers are described in Remington's Pharmaceutical Sciences, Mack Publishing Company, a standard reference text in this field.

Representative useful pharmaceutical dosage-forms for administration of the compounds of this invention can be illustrated as follows:

Capsules

A large number of unit capsules are prepared by filling standard two-piece hard gelatin capsules each with 100 milligrams of powdered active ingredient, 150 milligrams of lactose, 50 milligrams of cellulose, and 6 milligrams magnesium stearate.

Soft Gelatin Capsules

A mixture of active ingredient in a digestable oil such as soybean oil, cottonseed oil or olive oil is prepared and injected by means of a positive displacement pump into gelatin to form soft gelatin capsules containing 100 milligrams of the active ingredient. The capsules are washed and dried.

Tablets

A large number of tablets are prepared by conventional procedures so that the dosage unit is 100 milligrams of active ingredient, 0.2 milligrams of colloidal silicon dioxide, 5 milligrams of magnesium stearate, 275 milligrams of microcrystalline cellulose, 11 milligrams of starch and 98.8 milligrams of lactose. Appropriate coatings may be applied to increase palatability or delay absorption.

Injectable

A parenteral composition suitable for administration by injection is prepared by stirring 1.5% by weight of active ingredient in 10% by volume propylene glycol and water. The solution is made isotonic with sodium chloride and sterilized.

Suspension

An aqueous suspension is prepared for oral administration so that each 5 mL contain 100 mg of finely divided active ingredient, 200 mg of sodium carboxymethyl

cellulose, 5 mg of sodium benzoate, 1.0 g of sorbitol solution, U.S.P., and 0.025 mL of vanillin.

Where the compounds of this invention are combined with other anticoagulant agents, for example, a daily dosage may be about 0.1 to 100 milligrams of the compound of Formula I and about 1 to 7.5 milligrams of the second anticoagulant, per kilogram of patient body weight. For a tablet dosage form, the compounds of this invention generally may be present in an amount of about 5 to 10 milligrams per dosage unit, and the second anti-coagulant in an amount of about 1 to 5 milligrams per dosage unit.

Where the compounds of Formula I are administered in combination with an anti-platelet agent, by way of general guidance, typically a daily dosage may be about 0.01 to 25 milligrams of the compound of Formula I and about 50 to 150 milligrams of the anti-platelet agent, preferably about 0.1 to 1 milligrams of the compound of Formula I and about 1 to 3 milligrams of antiplatelet agents, per kilogram of patient body weight.

Where the compounds of Formula I are adminstered in combination with thrombolytic agent, typically a daily dosage may be about 0.1 to 1 milligrams of the compound of Formula I, per kilogram of patient body weight and, in the case of the thrombolytic agents, the usual dosage of the thrombolyic agent when administered alone may be reduced by about 70-80% when administered with a compound of Formula I.

Where two or more of the foregoing second therapeutic agents are administered with the compound of Formula I, generally the amount of each component in a typical daily dosage and typical dosage form may be reduced relative to the usual dosage of the agent when administered alone, in view of the additive or synergistic effect of the therapeutic agents when administered in combination.

Particularly when provided as a single dosage unit, the potential exists for a chemical interaction between the combined active ingredients. For this reason, when the compound of Formula I and a second therapeutic agent are combined in a single dosage unit they are formulated such that

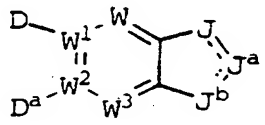
although the active ingredients are combined in a single dosage unit, the physical contact between the active ingredients is minimized (that is, reduced). For example, one active ingredient may be enteric coated. By enteric coating one of the active ingredients, it is possible not only to minimize the contact between the combined active ingredients, but also, it is possible to control the release of one of these components in the gastrointestinal tract such that one of these components is not released in the stomach but rather is released in the intestines. One of the active ingredients may also be coated with a material which effects a sustained-release throughout the gastrointestinal tract and also serves to minimize physical contact between the combined active ingredients. Furthermore, the sustained-released component can be additionally enteric coated such that the release of this component occurs only in the intestine. Still another approach would involve the formulation of a combination product in which the one component is coated with a sustained and/or enteric release polymer, and the other component is also coated with a polymer such as a lowviscosity grade of hydroxypropyl methylcellulose (HPMC) or other appropriate materials as known in the art, in order to further separate the active components. The polymer coating serves to form an additional barrier to interaction with the other component.

These as well as other ways of minimizing contact between the components of combination products of the present invention, whether administered in a single dosage form or administered in separate forms but at the same time by the same manner, will be readily apparent to those skilled in the art, once armed with the present disclosure.

Obviously, numerous modifications and variations of the present invention are possible in light of the above teachings. It is therefore to be understood that within the scope of the appended claims, the invention may be practiced otherwise that as specifically described herein.

WHAT IS CLAIMED AS NEW AND DESIRED TO BE SECURED BY LETTER PATENT OF UNITED STATES IS:

1. A compound of formula I:



I

or stereoisomer or pharmaceutically acceptable salt form thereof wherein:

W and W^3 are selected from CH and N;

W^1 and W^2 are selected from C, CH, and N;

provided that from 0-2 of W, W^1, W^2, and W^3 are N;

one of D and D^a is selected from H, C_{1-4} alkoxy, CN, $C(=NR^7)NR^8R^9$, $NHC(=NR^7)NR^8R^9$, $NR^8CH(=NR^7)$, $C(O)NR^8R^9$, and $(CH_2)_tNR^8R^9$, and the other is absent;

provided that if one of D and D^a is H, then at least one of W, W^1, W^2, and W^3 is N;

one of J^a and J^b is substituted by $-(CH_2)_n-Z-A-B$;

J, J^a, and J^b combine to form an aromatic heterocyclic system containing from 1-2 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^1, provided that J^b can only be C or N;

J, J^a, and J^b can, alternatively, combine to form a heterocyclic ring wherein J^b is N and J and J^a are CH_2 substituted with 0-1 R^1;

J, J^a, and J^b can, alternatively, combine to form a heterocyclic ring wherein J^b is CH, J is NR^1 and J^a is CH_2 substituted with 0-1 R^1;

R^1 is selected from H, C_{1-4} alkyl, $(CH_2)_rOR^3$, $(CH_2)_rNR^3R^{3'}$, $(CH_2)_rC(=O)R^2$, $(CH_2)_r(CH=CH)(CH_2)_rC(=O)R^2$, $(CH_2)_rNR^3C(=O)R^2$, $(CH_2)_rSO_2R^4$, $(CH_2)_rNR^3SO_2R^4$, and $(CH_2)_r$-5-membered heterocyclic system having 1-4 heteroatoms selected from N, O, and S;

R^2 is selected from H, OR^3, C_{1-4} alkyl, $NR^3R^{3'}$, CF_3, and C_{3-10} carbocyclic residue substituted with 0-2 R^6;

R^3 and $R^{3'}$ are independently selected from H, C_{1-4} alkyl, and C_{3-10} carbocyclic residue substituted with 0-2 R^6;

R^4 is selected from C_{1-4} alkyl, $NR^3R^{3'}$, and C_{3-10} carbocyclic residue substituted with 0-2 R^6;

Z is selected from CH=CH, $CH((CH_2)_mQ(CH_2)_mR^5)$, $CH((CH_2)_mQ(CH_2)_mR^5)C(O)NR^3$, $CH((CH_2)_mC(O)(CH_2)_mR^{5a})$, $N((CH_2)_qQ(CH_2)_mR^5)$, $N(Q'(CH_2)_mR^5)$, $C(O)N((CH_2)_mQ'(CH_2)_mR^{5a})$, $C(O)(CH_2)_r$, $C(O)O(CH_2)_r$, $OC(O)(CH_2)_r$, $C(O)(CH_2)_rNR^3(CH_2)_r$, $NR^3C(O)(CH_2)_r$, $OC(O)NR^3(CH_2)_r$, $NR^3C(O)O(CH_2)_r$, $NR^3C(O)NR^3(CH_2)_r$, $S(O)_p(CH_2)_r$, SO_2CH_2, $SCH_2C(O)NR^3$, $SO_2NR^3(CH_2)_r$, $NR^3SO_2(CH_2)_r$, and $NR^3SO_2NR^3(CH_2)_r$;

Q is selected from a bond, O, NR^3, C(O), $C(O)NR^3$, $NR^3C(O)$, SO_2, NR^3SO_2, and SO_2NR^3;

Q' is selected from a bond, C(O), $C(O)NR^3$, SO_2, and SO_2NR^3;

R^5 is selected from H, C_{1-4} alkyl, C_{3-10} carbocyclic residue substituted with 0-2 R^6, and 5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6,

provided that when Q is SO_2 or NR^3SO_2, R^5 is other than H and when Q' is SO_2, R^5 is other than H;

R^{5a} is selected from NHR^5, OR^5, and R^5;

A is selected from:

benzyl substituted with 0-2 R^6,

phenethyl substituted with 0-2 R^6,

phenyl-CH= substituted with 0-2 R^6,

C_{3-10} carbocyclic residue substituted with 0-2 R^6, and

5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

B is selected from:

X-Y, C_{3-6} alkyl, $NR^3R^{3'}$, $C(=NR^3)NR^3R^{3'}$, $NR^3C(=NR^3)NR^3R^{3'}$,

benzyl substituted with 0-2 R^6,

C_{3-10} carbocyclic residue substituted with 0-2 R^6, and

5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

A and B can, alternatively, combine to form a C_{9-10} carbocyclic residue substituted with 0-2 R^6 or a 9-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

X is selected from C_{1-4} alkylene, $-C(O)-$, $-C(O)CR^3R^{3'}-$, $-CR^3R^{3'}C(O)$, $-S(O)_p-$, $-S(O)_pCR^3R^{3'}-$, $-CR^3R^{3'}S(O)_p-$, $-S(O)_2NR^3-$, $-NR^3S(O)_2-$, $-C(O)NR^3-$, $-NR^3C(O)-$, $-NR^3-$, $-NR^3CR^3R^{3'}-$, $-CR^3R^{3'}NR^3-$, O, $-CR^3R^{3'}O-$, and $-OCR^3R^{3'}-$;

Y is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^6, and

5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

R^6 is selected from H, OH, $(CH_2)_nOR^3$, halo, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^3R^{3'}$, $(CH_2)_rC(O)R^3$, $NR^3C(O)R^{3'}$, $NR^3C(O)NR^3R^{3'}$, $CH(=NH)NH_2$, $NHC(=NH)NH_2$, $SO_2NR^3R^{3'}$, $CONHSO_2R^4$, $NR^3SO_2NR^3R^{3'}$, NR^3SO_2-C_{1-4} alkyl, and (C_{1-4} alkyl)-tetrazolyl;

R^7 is selected from H, OH, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkoxy, C_{1-4} alkoxycarbonyl, C_{6-10} aryloxy, C_{6-10} aryloxycarbonyl, C_{6-10} arylmethylcarbonyl, C_{1-4} alkylcarbonyloxy C_{1-4} alkoxycarbonyl, C_{6-10} arylcarbonyloxy C_{1-4} alkoxycarbonyl, C_{1-6} alkylaminocarbonyl, phenylaminocarbonyl, and phenyl C_{1-4} alkoxycarbonyl;

R^8 is selected from H, C_{1-6} alkyl and $(CH_2)_n$-phenyl;

R^9 is selected from H, C_{1-6} alkyl and $(CH_2)_n$-phenyl;

n is selected from 0, 1, 2, 3, and 4;

m is selected from 0, 1, and 2;

p is selected from 0, 1, and 2;

q is selected from 1 and 2; and,

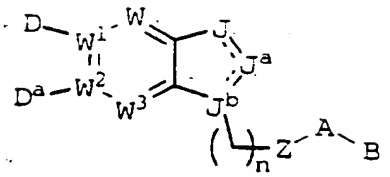
r is selected from 0, 1, 2, 3, and 4;

provided that:

(a) Z is other than CH_2; and,

(b) if Z is $CH((CH_2)_mQ(CH_2)_mR^5)$ or $CH((CH_2)_mC(O)(CH_2)_mR^{5a})$, then B is other than X-Y, a C_{3-10} carbocyclic residue or a 5-10 membered heterocyclic system.

2. A compound according to Claim 1, wherein the compound is of formula II:



II

or a stereoisomer or pharmaceutically acceptable salt, wherein:

from 0-1 of W, W^1, W^2, and W^3 are N;

R^1 is selected from H, C_{1-4} alkyl, $(CH_2)_rOR^3$, $(CH_2)_rNR^3R^{3'}$, $(CH_2)_rC(=O)R^2$, $(CH_2)_rNR^3C(=O)R^2$, $(CH_2)_rSO_2R^4$, $(CH_2)_rNR^3SO_2R^4$, and $(CH_2)_r$-5-membered heterocyclic system having 1-4 heteroatoms selected from N, O, and S;

R^2 is selected from H, OR^3, C_{1-4} alkyl, $NR^3R^{3'}$, and CF_3;

R^3 and $R^{3'}$ are independently selected from H, C_{1-4} alkyl, and phenyl;

R^4 is selected from C_{1-4} alkyl, phenyl and $NR^3R^{3'}$;

Z is selected from CH=CH, $CH((CH_2)_mQ(CH_2)_mR^5)$, $CH((CH_2)_mQ(CH_2)_mR^5)C(O)NR^3$, $CH((CH_2)_mC(O)(CH_2)_mR^{5a})$, $N((CH_2)_qQ(CH_2)_mR^5)$, $N(Q'(CH_2)_mR^5)$, $C(O)N((CH_2)_mQ'(CH_2)_mR^{5a})$, C(O), $C(O)CH_2$, C(O)O, OC(O), $C(O)(CH_2)_rNR^3(CH_2)_r$, $NR^3C(O)$, $OC(O)NR^3$, $NR^3C(O)O$, $NR^3C(O)NR^3$, $S(O)_p$, SO_2CH_2, SO_2NR^3, NR^3SO_2, and $NR^3SO_2NR^3$;

B is selected from:

X-Y, C_{3-6} alkyl,

benzyl substituted with 0-2 R^6,

C_{3-10} carbocyclic residue substituted with 0-2 R^6, and

5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

A and B can, alternatively, combine to form a C_{9-10} carbocyclic residue substituted with 0-2 R^6 or a 9-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6; and,

R^6 is selected from H, OH, $(CH_2)_nOR^3$, halo, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^3R^{3'}$, $(CH_2)_rC(O)R^3$, $NR^3C(O)R^{3'}$, $NR^3C(O)NR^3R^{3'}$, $SO_2NR^3R^{3'}$, $CONHSO_2R^4$, $NR^3SO_2NR^3R^{3'}$, NR^3SO_2-C_{1-4} alkyl and (C_{1-4} alkyl)-tetrazolyl.

3. A compound according to Claim 2, wherein:

J, J^a, and J^b combine to form an aromatic heterocyclic system containing from 1-2 nitrogen atoms, substituted with 0-1 R^1;

J, J^a, and J^b can, alternatively, combine to form a heterocyclic ring wherein J^b is N and J and J^a are CH_2 substituted with 0-1 R^1;

J, J^a, and J^b can, alternatively, combine to form a heterocyclic ring wherein J^b is CH, J is NR^1 and J^a is CH_2 substituted with 0-1 R^1;

R^1 is selected from H, C_{1-4} alkyl, $(CH_2)_rOR^3$, $(CH_2)_rNR^3R^{3'}$, $(CH_2)_rC(=O)R^2$, $(CH_2)_rNR^3C(=O)R^2$, $(CH_2)_rSO_2R^4$, and $(CH_2)_rNR^3SO_2R^4$;

Z is selected from $CH((CH_2)_mQ(CH_2)_mR^5)$, $CH((CH_2)_mQ(CH_2)_mR^5)C(O)NR^3$, $CH((CH_2)_mC(O)(CH_2)_mR^{5a})$, $N((CH_2)_qQ(CH_2)_mR^5)$, $N(Q'(CH_2)_mR^5)$, $C(O)N((CH_2)_mQ'(CH_2)_mR^{5a})$, $C(O)$, $C(O)CH_2$, $C(O)(CH_2)_rNR^3(CH_2)_r$, $NR^3C(O)$, $NR^3C(O)NR^3$, $S(O)_2$, SO_2CH_2, SO_2NR^3, NR^3SO_2, and $NR^3SO_2NR^3$;

A is selected from:

benzyl substituted with 0-2 R^6,

C_{3-10} carbocyclic residue substituted with 0-2 R^6, and

5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

B is selected from:

X-Y, C_{3-6} alkyl,

benzyl substituted with 0-2 R^6,

C_{5-6} carbocyclic residue substituted with 0-2 R^6, and

5-6 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

X is selected from $-C(O)-$, $-C(O)CR^3R^{3'}-$, $-S(O)_2-$, $-S(O)_pCR^3R^{3'}-$, $-S(O)_2NR^3-$, $-C(O)NR^3-$, $-NR^3-$, $-NR^3CR^3R^{3'}-$, and O;

Y is selected from:

C_{5-6} carbocyclic residue substituted with 0-2 R^6, and

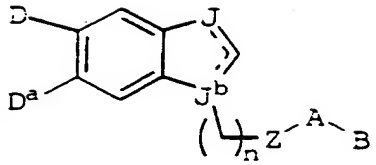
5-6 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

R^6 is selected from H, OH, $(CH_2)_nOR^3$, halo, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^3R^{3'}$, $(CH_2)_rC(O)R^3$, $NR^3C(O)R^{3'}$, $NR^3C(O)NR^3R^{3'}$, $SO_2NR^3R^{3'}$, $CONHSO_2R^4$, $NR^3SO_2NR^3R^{3'}$, NR^3SO_2-C_{1-4} alkyl and (C_{1-4} alkyl)-tetrazolyl;

n is selected from 0, 1, and 2; and,

r is selected from 0, 1, and 2.

4. A compound according to Claim 3, wherein the compound is of formula II:



III

or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

J and J^b combine to form an aromatic heterocyclic system containing from 1-2 nitrogen atoms, substituted with 0-1 R^1;

J and J^b can, alternatively, form a heterocyclic ring wherein J^b is N and J is CH_2 substituted with 0-1 R^1;

J and J^b can, alternatively, form a heterocyclic ring wherein J^b is CH and J is NR^1;

Z is selected from $C(O)N(Q'R^{5a})$, $C(O)$, $C(O)NR^3$, $NR^3C(O)$, and SO_2NR^3;

Q' is selected from $C(O)$ and $C(O)NR^3$;

R^5 is selected from H and C_{1-4} alkyl;

R^{5a} is selected from NHR^5, OR^5, and R^5;

A is selected from:
benzyl substituted with 0-1 R^6,
phenyl substituted with 0-1 R^6,
piperidinyl substituted with 0-1 R^6,
piperazinyl substituted with 0-1 R^6, and
pyridyl substituted with 0-1 R^6;

B is selected from:
X-Y,
benzyl substituted with 0-1 R^6,
phenyl substituted with 0-2 R^6,

cyclohexyl substituted with 0-1 R^6, and
pyridyl substituted with 0-1 R^6;

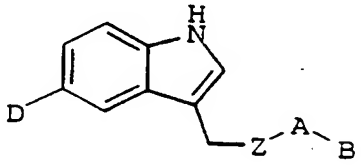
X is selected from: $-C(O)-$, $-S(O)_2-$, SO_2CH_2, $-S(O)_2NR^3-$, $-NR^3-$ and $-C(O)NR^3-$;

Y is selected from:
phenyl substituted with 0-2 R^6, and
pyridyl substituted with 0-1 R^6;

R^6 is selected from H, OH, $(CH_2)_nOR^3$, halo, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^3R^{3'}$, $(CH_2)_rC(O)R^3$, $NR^3C(O)R^{3'}$, $NR^3C(O)NR^3R^{3'}$, $SO_2NR^3R^{3'}$, $CONHSO_2R^4$, $NR^3SO_2NR^3R^{3'}$, NR^3SO_2-C_{1-4} alkyl and (C_{1-4} alkyl)-tetrazolyl;

n is selected from 0, 1, and 2.

5. A compound according to Claim 4, wherein the compound is of of formula IV:



IV

or stereoisomer or pharmaceutically acceptable salt form thereof, wherein A, B, D, and Z are as defined above.

6. A compound according to Claim 1, wherein the compound is selected from:

3-((4-cyclohexyl)phenylaminomethylcarbonyl)methyl-5-amidinoindole

3-(4-p-toluenesulfonyl-piperazinecarbonyl)methyl-5-amidinoindole

3-(4-(2-aminosulfonylphenyl)pyridine-2-aminocarbonyl)methyl-5-amidinoindole;

3-(4-[2-tetrazole]phenyl)phenylaminocarbonyl)methyl-5-amidinoindole;

3-(4-biphenylaminocarbonyl)methyl-5-amidinoindole;

3-(4-(phenylmethylsulfonyl)piperazinecarbonyl)methyl-5-amidinoindole;

3-(4-cyclohexylphenylaminocarbonyl)methyl-5-amidinoindole;

3-(4-benzylpiperazinecarbonyl)methyl-5-amidinoindole;

3-(3-amidinobenzylamino(methylcarbonylmethoxy)carbonyl)methyl-5-amidinoindole;

3-(4-[2-aminosulfonyl)phenylphenylaminocarbonyl)methyl-5-amidinoindole;

3-(1-benzylpiperidine-4-aminocarbonyl)methyl-5-amidinoindole;

3-(4-phenylpiperazinecarbonyl)methyl-5-amidinoindole;

3-(4-benzylpiperidinecarbonyl)methyl-5-amidinoindole;

3-(2-bromo-4-(2-aminosulfonyl)phenylphenylaminocarbonyl)methyl-5-cyanoindole;

3-(2-methyl-4-(2-aminosulfonyl)phenylphenylaminocarbonyl)methyl-5-methylamino indole;

3-{2-fluoro-4-(2-aminosulfonyl)phenylphenylaminocarbonyl)methyl-5-amidnoindole;

3-{2-chloro-4-(2-aminosulfonyl)phenylphenylaminocarbonyl)methyl-5-cyanoindole;

3-{2-iodo-4-(2-aminosulfonyl)phenylphenylaminocarbonyl)methyl-5-cyanoindole;

3-{2-methyl-4-(2-aminosulfonyl)phenylphenylaminocarbonyl)methyl-5-amidinoindole;

3-{2-methyl-4-(2-(t-butylaminosulfonyl))phenylphenylaminocarbonyl)methyl-5-amidinoindole;

3-{4-(2-aminosulfonyl)phenyl)phenylaminocarbonylmethyl-α-(methylcarboxy methylether)-5-amidinoindole;

3-{4-(2-aminosulfonyl)phenyl)phenylaminocarbonylmethyl-α-(benzyl)-5-amidinoindole;

3-{4-(2-trifluoromethyl)phenyl)pyrid-2-ylaminocarbonylmethyl-5-amidinoindole;

3-{4-(2-ethylaminosulfonyl)phenyl)phenylaminocarbonylmethyl-5-amidinoindole;

3-{4-(2-propylaminosulfonyl)phenyl)phenyl}aminocarbonylmethyl-5-amidinoindole;

2-methyl-3-{2-iodo-4-(2-aminosulfonyl)phenyl)phenyl}aminocarbonylmethyl-5-amidinoindole;

2-methyl-3-{4-(2-aminosulfonyl)phenyl)phenyl}aminocarbonylmethyl-5-amidinoindole;

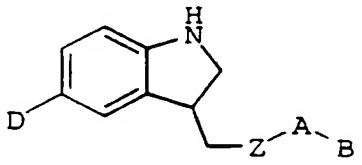
3-{4-(2-aminosulfonyl)phenyl)phenyl}-N-methylaminocarbonylmethyl-5-amidinoindole;

2-methyl-3-{4-(2-t-butylaminosulfonyl)phenyl)phenyl}aminocarbonylmethyl-5-methoxyindole; and,

3-{4-(2-N-methylaminosulfonyl)phenyl)phenyl}-N-methylaminocarbonylmethyl-5-amidinoindole;

or a stereoisomer or pharmaceutically acceptable salt form thereof.

7. A compound according to Claim 4, wherein the compound is of formula IVa:



IVa

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein A, B, D, and Z are as defined above.

8. A compound according to Claim 1, wherein the compound is selected from:

3-{4-(2-(n-butylaminosulfonyl)phenylphenylaminocarbonyl)methyl-5-cyanoindoline;

3-{4-(2-(n-propylaminosulfonyl)phenylphenylaminocarbonyl)methyl-5-amidinoindoline;

(-)-3-{4-(2-aminosulfonyl)phenyl)pyrid-2-ylaminocarbonylmethyl-5-amidinoindoline;

3-{4-(2-aminosulfonyl)phenyl)pyrid-2-ylaminocarbonylmethyl-5-amidinoindoline;

3-{4-(2-dimethylaminosulfonyl)phenyl)phenylaminocarbonylmethyl-5-amidinoindoline;

(+)-3-{4-(2-t-butylaminosulfonyl)phenyl)pyrid-2-ylaminocarbonylmethyl-5-amidinoindoline;

(-)-3-{4-(2-t-butylaminosulfonyl)phenyl)pyrid-2-ylaminocarbonylmethyl-5-amidinoindoline;

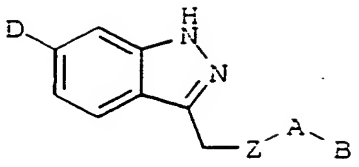
3-{4-(2-aminosulfonyl)phenyl)pyrid-2-yl)aminocarbonylmethyl-5-aminocarboxyindoline;

3-{4-(2-t-butylaminosulfonyl)phenyl)phenyl)aminocarbonylmethyl-5-amidinoindoline; and,

3-{4-(2-t-butylaminosulfonyl)phenyl)pyrid-2-yl)aminocarbonylmethyl-5-amidinoindoline;

or a stereoisomer or pharmaceutically acceptable salt form thereof.

9. A compound according to Claim 4, wherein the compound is of formula IVb:



IVb

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein A, B, D, and Z are as defined above.

10. A compound according to Claim 1, wherein the compound is selected from:

3-{4-(2-aminosulfonyl)phenyl)pyrid-2-ylaminocarbonylmethyl-6-amidinoindazole;

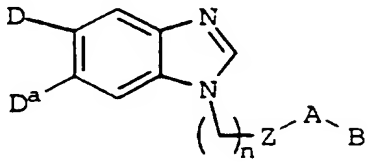
3-{4-(2-aminosulfonyl)phenyl)phenyl aminocarbonylmethyl-6-amidinoindazole;

3-{4-(2-t-butyl aminosulfonyl)phenyl)pyrid-2-ylaminocarbonylmethyl-6-amidinoindazole; and,

3-{4-(2-t-butylaminosulfonyl)phenyl)phenyl aminocarbonylmethyl-6-amidinoindazole; and,

or a stereoisomer or pharmaceutically acceptable salt form thereof.

11. A compound according to Claim 4, wherein the compound is of of formula IVc:



IVc

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein D, D^a, Z, A, and B are as defined above.

12. A compound according to Claim 1, wherein the compound is selected from:

[4-(phenyl)phenylcarbonyl]methyl-6-amidinobenzimidazole;

[4-(phenyl)phenylcarbonyl]methyl-5-amidinobenzimidazole;

[4-(3-aminophenyl)phenylcarbonyl]methyl-6-amidinobenzimidazole;

[4-(3-aminophenyl)phenylcarbonyl]methyl-5-amidinobenzimidazole;

[4-(4-fluorophenyl)phenylcarbonyl]methyl-6-amidinobenzimidazole;

[4-(4-formylphenyl)phenylcarbonyl]methyl-6-amidinobenzimidazole;

[4-(2-aminosulfonylphenyl)phenylcarbonyl]methyl-6-amidinobenzimidazole;

[4-(2-*tert*-butylaminosulfonylphenyl)phenylcarbonyl]methyl-6-amidinobenzimidazole;

{4-[(2-tetrazolyl)phenyl]phenylcarbonyl}methyl-6-amidinobenzimidazole;

[4-(2-aminosulfonylphenyl)phenylaminocarbonyl]methyl-6-amidinobenzimidazole;

[4-(2-aminosulfonylphenyl)phenylaminocarbonyl]methyl-5-amidinobenzimidazole;

1-(4-benzylpiperidinecarbonyl)methyl-6-amidinobenzimidazole;

1-(4-benzylpiperidinecarbonyl)methyl-5-amidinobenzimidazole;

1-(4-benzylpiperidinecarbonyl)methyl-6-amidinobenzimidazole; and,

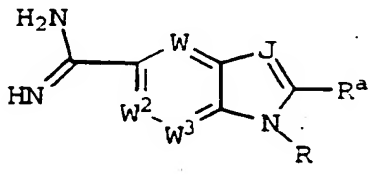
2-[4-(2-tert-butylaminosulfonylphenyl)phenylcarbonyl]methyl-5-azabenzimidazole;

2S-[4-(2-tert-aminosulfonylphenyl)phenylaminocarbonyl]methyl-thio-1H-imidazo(4,5-C) pyridine; and,

2S-[4-(2-aminosulfonylphenyl)phenylaminocarbonyl]methyl-thio-1H-imidazo(4,5-C) pyridine;

or a stereoisomer or pharmaceutically acceptable salt form thereof.

13. A compound according to Claim 1, or a stereoisomer or pharmaceutically acceptable salt thereof, wherein the compound is of formula V:



V

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein one of R and R^a is $-(CH_2)_n-Z-A-B$ and the other H;

W, W^2, and W^3 are selected from CH and N, provided that at most one of W, W^2, and W^3 can be N;

J is selected from N and C-R^1;

R^1 is selected from H, O, $(CH_2)_rOR^3$, $(CH_2)_rC(=O)R^2$, $(CH=CH)C(=O)R^2$, $(CH_2)_rNR^3C(=O)R^2$, $(CH_2)_rSO_2R^4$, $(CH_2)_rNR^3SO_2R^4$, and $(CH_2)_r$-5-membered heterocyclic system having 1-4 heteroatoms selected from N, O, and S;

R^2 is selected from H, OR^3, C_{1-4} alkyl, $NR^3R^{3'}$, CF_3, and C_{3-10} carbocyclic residue substituted with 0-2 R^6;

R^3 and $R^{3'}$ are independently selected from H, C_{1-4} alkyl, and C_{3-10} carbocyclic residue substituted with 0-2 R^6;

R^4 is selected from OR^3, C_{1-4} alkyl, $NR^3R^{3'}$, and C_{3-10} carbocyclic residue substituted with 0-2 R^6;

Z is selected from CH=CH, $CH(CH_2)_mQ(CH_2)_mR^5$, $CH((CH_2)_mQ(CH_2)_mR^5)C(O)NR^3$, $CH(CH_2)_mC(O)(CH_2)_mR^{5a}$, $N(CH_2)_qQ(CH_2)_mR^5$, $NQ'(CH_2)_mR^5$, $C(O)N((CH_2)_mQ'(CH_2)_mR^{5a})$, C(O), $C(O)CH_2$, C(O)O, OC(O), $C(O)NR^3(CH_2)_r$, $NR^3C(O)$, $OC(O)NR^3$, $NR^3C(O)O$, $NR^3C(O)NR^3$, $S(O)_p$, SO_2CH_2, SO_2NR^3, NR^3SO_2, and $NR^3SO_2NR^3$;

Q is selected from a bond, O, NR^3, C(O), $C(O)NR^3$, $NR^3C(O)$, SO_2, NR^3SO_2, and SO_2NR^3;

Q' is selected from a bond, C(O), $C(O)NR^3$, SO_2, and SO_2NR^3;

R^5 is selected from H, C_{1-4} alkyl, C_{3-8} carbocyclic residue substituted with 0-2 R^6, and 5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6, provided that when Q is SO_2 or NR^3SO_2, R^5 is other than H and when Q' is SO_2, R^5 is other than H;

R^{5a} is selected from NHR^5, OR^5, and R^5;

A is selected from:
benzyl substituted with 0-2 R^6,
C_{3-10} carbocyclic residue substituted with 0-2 R^6, and

5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

B is selected from:
H, X-Y, $NR^3R^{3'}$, $C(=NR^3)NR^3R^{3'}$, $NR^3C(=NR^3)NR^3R^{3'}$,
benzyl substituted with 0-2 R^6,
C_{3-10} carbocyclic residue substituted with 0-2 R^6, and
5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

X is selected from C_{1-4} alkylene, $-C(O)-$, $-C(O)CR^3R^{3'}-$, $-CR^3R^{3'}C(O)$, $-S(O)_p-$, $-S(O)_pCR^3R^{3'}-$, $-CR^3R^{3'}S(O)_p-$, $-S(O)_2NR^3-$, $-NR^3S(O)_2-$, $-C(O)NR^3-$, $-NR^3C(O)-$, $-NR^3-$, $-NR^3CR^3R^{3'}-$, $-CR^3R^{3'}NR^3-$, O, $-CR^3R^{3'}O-$, and $-OCR^3R^{3'}-$;

Y is selected from:
C_{3-10} carbocyclic residue substituted with 0-2 R^6, and
5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

R^6 is selected from H, OH, $(CH_2)_nOR^3$, halo, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^3R^{3'}$, $(CH_2)_rC(O)R^3$, $NR^3C(O)R^{3'}$, $NR^3C(O)NR^3R^{3'}$, $CH(=NH)NH_2$, $NHC(=NH)NH_2$, $C(=O)R^3$, $SO_2NR^3R^{3'}$, $NR^3SO_2NR^3R^{3'}$, and NR^3SO_2-C_{1-4} alkyl;

n is selected from 0, 1, 2, 3, and 4;

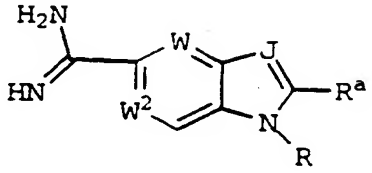
m is selected from 0, 1, and 2;

p is selected from 0, 1, and 2;

q is selected from 1 and 2; and,

r is selected from 0, 1, 2, 3, and 4.

14. A compound according to Claim 13, wherein the compound is of formula VI:



VI

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein one of R and R^a is $-(CH_2)_n-Z-A-B$ and the other H;

W and W^2 are selected from CH and N, provided that at most one of W and W^2 can be N;

J is selected from N and $C-R^1$;

R^1 is selected from H, $(CH_2)_rOR^3$, $(CH_2)_rC(=O)R^2$, $(CH_2)_rNR^3C(=O)R^2$, $(CH=CH)C(=O)R^2$, $(CH_2)_rSO_2R^4$, and $(CH_2)_rNR^3SO_2R^4$;

R^2 is selected from H, OR^3, C_{1-4} alkyl, $NR^3R^{3'}$, and CF_3;

R^3 and $R^{3'}$ are independently selected from H, C_{1-4} alkyl, and phenyl;

R^4 is selected from OR^3, C_{1-4} alkyl, $NR^3R^{3'}$, and phenyl;

Z is selected from C(O), $C(O)CH_2$, $C(O)NR^3$, $NR^3C(O)$, $S(O)_2$, SO_2CH_2, SO_2NR^3, NR^3SO_2, and $NR^3SO_2NR^3$;

A is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^6, and

5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

B is selected from:

X-Y,

C_{3-10} carbocyclic residue substituted with 0-2 R^6, and

5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

X is selected from -C(O)-, $-C(O)CR^3R^{3'}-$, $-CR^3R^{3'}C(O)$, $-S(O)_p-$, $-S(O)_pCR^3R^{3'}-$, $-CR^3R^{3'}S(O)_p-$, $-S(O)_2NR^3-$, $-NR^3S(O)_2-$, $-C(O)NR^3-$, $-NR^3-$, $-NR^3CR^3R^{3'}-$, and $-CR^3R^{3'}NR^3-$;

Y is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^6, and

5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

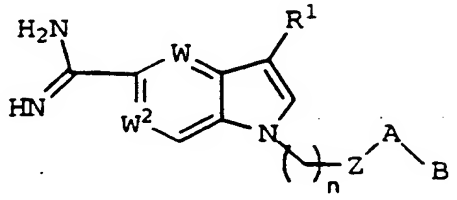
R^6 is selected from H, OH, $(CH_2)_nOR^3$, halo, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^3R^{3'}$, $(CH_2)_rC(O)R^3$, $NR^3C(O)R^{3'}$, $NR^3C(O)NR^3R^{3'}$, $C(=O)R^3$, $SO_2NR^3R^{3'}$, $NR^3SO_2NR^3R^{3'}$, and NR^3SO_2-C_{1-4} alkyl;

n is selected from 0, 1, 2, 3, and 4;

p is selected from 0, 1, and 2; and,

r is selected from 0, 1, 2, 3, and 4.

15. A compound according to Claim 14, wherein the compound is of formula VII:



VII

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein, W and W^2 are selected from CH and N, provided that at most one of W and W^2 can be N;

R^1 is selected from H, $(CH_2)_rOR^3$, $(CH_2)_rC(=O)R^2$, $(CH_2)_rNR^3C(=O)R^2$, $(CH=CH)C(=O)R^2$, $(CH_2)_rSO_2R^4$, and $(CH_2)_rNR^3SO_2R^4$;

R^2 is selected from H, OR^3, C_{1-4} alkyl, $NR^3R^{3'}$, and CF_3;

R^3 and $R^{3'}$ are independently selected from H, C_{1-4} alkyl, and phenyl;

R^4 is selected from OR^3, C_{1-4} alkyl, $NR^3R^{3'}$, and phenyl;

Z is selected from C(O), $C(O)CH_2$, $C(O)NR^3$, $S(O)_2$, SO_2CH_2, SO_2NR^3, and $NR^3SO_2NR^3$;

A is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^6, and

5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

B is selected from:

X-Y,

C_{3-10} carbocyclic residue substituted with 0-2 R^6, and

5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

X is selected from $-S(O)_p-$, $-S(O)_pCR^3R^{3'}-$, $-CR^3R^{3'}S(O)_p-$, $-S(O)_2NR^3-$, $-NR^3S(O)_2-$, and $-C(O)NR^3-$;

Y is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^6, and

5-10 membered heterocyclic system containing from 1-3 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^6;

R^6 is selected from H, OH, $(CH_2)_nOR^3$, halo, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^3R^{3'}$, $(CH_2)_rC(O)R^3$, $NR^3C(O)R^{3'}$, $NR^3C(O)NR^3R^{3'}$, $C(=O)R^3$, $SO_2NR^3R^{3'}$, $NR^3SO_2NR^3R^{3'}$, and NR^3SO_2-C_{1-4} alkyl;

n is selected from 0, 1, 2, 3, and 4;

p is selected from 0, 1, and 2; and,

r is selected from 0, 1, 2, 3, and 4.

16. A compound according to Claim 13, wherein the compound is selected from:

1-(4-benzylpiperidinecarbonyl)methyl-5-amidinoindole;

1-(4-benzylpiperidinecarbonyl)ethyl-5-amidinoindole;

1-(4-(3-fluoro)benzylpiperidinecarbonyl)methyl-5-amidinoindole;

1-(1-(4-amidino)benzyl-N-(methylacetate)aminocarbonyl)methyl-5-amidinoindole;

methyl 1-(4-benzylpiperidinecarbonyl)methyl-5-amidinoindole-3-propanoate;

1-((4-benzylpiperidinecarbonyl)methyl-(3-ethanehydroxyl)-5-amidinoindole;

1-(4-benzylpiperidine-1-carbonyl)methyl-3-methylcarboxylic acid-5-amidinoindole;

1-(1-benzylpiperidine-4-aminocarbonyl)methyl-5-amidinoindole;

1-(4-benzoylpiperidinecarbonyl)methyl-5-amidinoindole;

1-(4-(3-fluoro)benzylpiperazinecarbonyl)methyl-5-amidinoindole;

1-(4-phenylbenzylaminocarbonyl)methyl-5-amidinoindole;

methyl 1-(4-benzylpiperidinecarbonyl)methyl-5-amidinoindole-3-propenoate; and,

1-(4-(2-fluoro)benzylpiperidinecarbonyl)methyl-5-amidinoindole;

or a stereoisomer or pharmaceutically acceptable salt form thereof.

17. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt thereof.

18. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound according to Claim 2 or a pharmaceutically acceptable salt thereof.

19. A method for treating or preventing a thromboembolic disorder, comprising: administering to a patient in need thereof a therapeutically effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt thereof.

20. A method for treating or preventing a thromboembolic disorder, comprising: administering to a patient in need thereof a therapeutically effective amount of a compound according to Claim 2 or a pharmaceutically acceptable salt thereof.